

# Department of Clinical Investigation

## *Annual Research Progress Report*



DTIC QUALITY INSPECTOR

**Fiscal Year 1997**  
Madigan Army Medical Center  
Tacoma, Washington

19980217 509

# REPORT DOCUMENTATION PAGE

Form Approved  
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE 30 Sept 97	3. REPORT TYPE AND DATES COVERED Annual 1 Oct 96 - 30 Sep 97	
4. TITLE AND SUBTITLE Annual Research Progress Report Department of Clinical Investigation			5. FUNDING NUMBERS	
6. AUTHOR(S) Nancy Whitten            Barbara Jones Troy Patience            Genie Hough				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Department of Clinical Investigation Madigan Army Medical Center Tacoma, WA 98431			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) Clinical Investigation Regulatory Office U.S. Army Medical Center and School Fort Sam Houston, TX 78234-6125			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words)  This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 97. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 97. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during FY 97.  <div style="text-align: right;">DTIC QUALITY INSPECTED</div>				
14. SUBJECT TERMS  Research protocols, investigators, objectives, progress, technical approach			15. NUMBER OF PAGES 629	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT UL	



**ANNUAL PROGRESS REPORT**

30 SEPTEMBER 1997

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

THE FINDINGS IN THIS REPORT ARE NOT TO BE  
CONSTRUED AS AN OFFICIAL DEPARTMENT OF THE  
ARMY POSITION UNLESS SO DESIGNATED BY OTHER  
AUTHORIZED DOCUMENTS.

DESTROY THIS REPORT WHEN NO LONGER NEEDED.  
DO NOT RETURN IT TO THE ORIGINATOR.

APPROVED FOR PUBLIC RELEASE  
DISTRIBUTION UNLIMITED

## TABLE OF CONTENTS

Introduction.....	1
Acknowledgements .....	1
Foreword .....	2
Unit Summary .....	3
Committee Members.....	7
Bryon L. Steger Research Award .....	8
Fellow's Research Award.....	9
Joyce Award.....	10
Publications .....	11
Presentations.....	18
Index To Protocols .....	27
Regular Protocols	
62nd Medical Group .....	63
Fort Lewis, Special Forces .....	65
United States Department of Agriculture.....	68
Department of Anesthesiology and Operative Services .....	70
Department of Clinical Investigation .....	72
Department of Dentistry.....	100
Department of Emergency Medicine.....	103
Department of Family Practice.....	120
Department of Medicine, Cardiology Service.....	135
Department of Medicine, Endocrinology Service.....	149
Department of Medicine, Gastroenterology Service.....	153
Department of Medicine, Hematology/Oncology Service.....	159
Department of Medicine, Infectious Disease Service .....	178
Department of Medicine, Internal Medicine Service.....	180
Department of Medicine, Neurology Service.....	192
Department of Medicine, Pulmonary Service.....	197
Department of Nursing .....	209
Department of Obstetrics/Gynecology .....	238
Department of Pediatrics.....	254

## TABLE OF CONTENTS (CONT'D)

Physical Medicine and Rehabilitation Service.....	265
Preventive Medicine Service.....	272
Department of Psychology.....	276
Department of Radiology.....	281
Department of Surgery, Cardiothoracic Surgery Service .....	295
Department of Surgery, General Surgery Service.....	297
Department of Surgery, Ophthalmology Service .....	318
Department of Surgery, Orthopedics Service.....	335
Department of Surgery, Otolaryngology Service .....	356
Department of Surgery, Urology Service.....	367
Department of Surgery, Vascular Surgery Service.....	392
Social Work Service .....	395
Cancer Group Protocols	
Gynecology Oncology Group.....	399
National Surgical Adjuvant Breast & Bowel Project.....	459
Pediatric Oncology Group.....	461
Radiological Diagnostic Oncology Group.....	500
Southwest Oncology Group.....	502
University of Washington Neuro-Oncology Group.....	610
Investigator Index.....	612
Keyword Index .....	619
Distribution .....	629

# ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1997

DEPARTMENT OF CLINICAL INVESTIGATION  
MADIGAN ARMY MEDICAL CENTER  
TACOMA, WASHINGTON 98431

## Introduction

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

## Acknowledgements

I would like to take this opportunity to thank Nancy Whitten, Barbara Jones, Troy Patience, and Genie Hough for their effort which is obvious in the compilation, preparation, and editing of this publication.

## Foreword

In FY 97 the number of new protocols submitted and total protocols managed by DCI continued to keep us very busy. During this FY, DCI processed 148 new protocols and managed 510 total protocols. MAMC investigators continued to attract clinical trials at an increasing rate, augmenting their extramural funding through multiple foundations. MAMC nurses were again successful in competing for Tri-service Nursing research funding, bringing in over \$270,000. Sixty-three investigators were trained in our biannual Introduction to Clinical Investigation Course, and the department continued its strong thrust in molecular biology, training 10 fellows and staff in MAMC's Short Course in Molecular Biology for Physicians. This course was exported to a Tri-service environment in FY 97 as CPT Wade Aldous coordinated a workshop "An Introduction to Molecular Biology" at the 21<sup>st</sup> annual meeting of the Society of Armed Forces Medical Laboratory Scientists. Several individual investigators have contributed to the department's well earned reputation as a leader in many fields of experimental biology. Dr. Kathy Moore continued to investigate the role of steroid binding protein in breast and prostate cancer, primarily using the tools of molecular biology. CPT Wade Aldous expanded his work on the enzyme telomerase to include investigation into its usefulness as an early marker for cancer and as a target for prevention of infection with malaria. CPT Aziz Qabar has continued his work on angiogenesis and the role of thrombospondins by using molecular tools to produce chimeric proteins to determine the protein motifs that determine the pro- and anti-angiogenic properties of the different thrombospondins. LTC Richard Sherman has been the research mentor to the Department of Surgery, guiding the development of a number of projects. In addition, he has continued his work in the fields of referred pain and treatment of migraine headaches. MAJ Ron Nielson, DVM, has ably supervised the increased laboratory animal research activity of Madigan's investigators. He has supported protocols utilizing animals ranging in size from mice to goats and sheep. MAJ Curtis Yeager continued to guide the Research Support Service until he moved on to become the Chief of Microbiology in the Department of Pathology. LTC C. Ray Dotson arrived to take over the Research Administrative Service (renamed Research Support Service) in DCI. Finally, this is my last annual report as I have completed over 20 years of service, and will retire from the Army in February of 1998. The friendships and professional acquaintances that I have made during my Army career, and during my tenure as Chief of Madigan's Department of Clinical Investigation will always be cherished. A search committee was appointed by the Command to choose my successor. I'm happy to report that they selected a fine replacement, LTC (P) Roderick F. Hume Jr., MC.

The support of BG George Brown, Commander, COL Darrell Porr and COL Casey Jones, DCCS, COL William Cahill, DCA and COL Patrick Kelly, Director of Medical Education are gratefully acknowledged for their roles in the department fulfilling its mission.

# Unit Summary

## 1. Objective

To provide the facilities and environment to stimulate an interest in clinical and basic investigations within Madigan Army Medical Center and its region.

## 2. Technical Approach

### Manpower

<u>Description</u>	<u>Rank</u>	<u>MOS</u>
Chief, Clinical Investigation MOORE, Dan C., M.D., COL, MC	O6	60P9A
Chief, Clinical Studies Service VACANT		
Director, Surgical Research Service SHERMAN, Richard A., Ph.D., LTC, MS	O5	71F67
Chief, Lab Animal & Surgery Service NEILSEN, Ronald E., D.V.M., MAJ, VC	O4	75C64
Chief, Research Administration Service YEAGER, Curtis L., Ph.D., MAJ, MS (PCS Jun 97)	O4	71A67
Chief, Research Administration Service DOTSON, Carroll Ray, LTC, MS (EOD Aug 97)	O5	71A67
Chief, BioResearch Service VACANT		
Chief, Microbiology Service ALDOUS, Wade K., Ph.D., CPT, MS	O3	71A67
Chief, Biochemistry Service QABAR, Aziz N., Ph.D., CPT, MS	O3	71B67
NCOIC HERNANDEZ, Carlos I., SFC (PCS Jun 97)	E7	91K4R
NCOIC TROTMAN, Ian C., SFC, MLT (EOD Jun 97)	E7	91K4R
Senior Animal Care Sgt. BARRETT, Vickie R., SFC, LATG	E7	91T4R
Senior Animal Care Sgt. BROWN, Bruce A., SGT	E5	91T2R

## Manpower (continued)

<u>Description</u>	<u>Rank</u>	<u>MOS</u>
Senior Animal Care Sgt HEATH, George, SGT (RET Aug 97)	E5	91T2R
Animal Care Specialist LONG, Brett W., SPC (P)	E4	91T10
Lab Tech KEENE, Corey A., SGT (ETS May 97)	E4	91K2R
Lab Tech SOLA, Milagros, SPC (PCS Apr 97)	E4	91K10
Lab Tech WILLIAMS, Iridiana, SGT, MLT (EOD Feb 97)	E4	91K10
Research Admin Scientist MOORE, Katherine H., Ph.D.	GS13	0601
Med Tech MATEJ, Louis A., B.S., MLT (ASCP)	GS11	0644
Med Tech WRIGHT, James R., B.A., MT (ASCP)	GS11	0644
Med Tech DEHART, M. J., B.S.	GS11	0644
Med Tech BULLOCK, Jeff M., M.S.	GS11	0644
Statistician (Medicine) PATIENCE, Troy H., B.S.	GS09	1530
Research Protocol Specialist WHITTEN, Nancy J., B.A.	GS09	1087
Clinical Research Associate JONES, Barbara A., A.A.	GS05	0303
Sec/Steno HOUGH, Eugenia R.	GS06	0318
Maintenance Worker KAEO, Curtis	WG7	4749

## Funding FY 97

Civilian Payroll	\$472,200
Military Payroll	\$573,876
Operations	\$98,400
CEEP	\$168,742
TDY	\$5,300
Services	\$-
<b>Total:</b>	<b>\$1,318,518</b>
 <b>MEDCASE:</b>	 <b>\$135,230</b>
 <b>Grants USAMRDC:</b>	 <b>\$10,000</b>
 Air Force	 \$12,926
Ft. Lewis	\$2,294
Pentagon	\$100,000
Triservice Nursing Research	\$272,118
POG	\$4,005
<b>Grants Federal:</b>	<b>\$391,343</b>
 FACT	 \$150
Geneva Foundation	\$332,047
Jackson Foundation	\$8,063
<b>Grants Non-federal:</b>	<b>\$332,197</b>
 <b>Grants Total:</b>	 <b>\$741,603</b>
 <b>FUNDING TOTAL:</b>	 <b>\$2,769,227</b>



### 3. Progress

During FY 97, there were 510 active protocols that received administrative and/or technical support during the year. Of these, 312 are presently ongoing, 14 are in a suspended status, 127 were completed, and 57 were terminated. The principal investigator distribution was as follows: 395 staff protocols (includes 192 group oncology protocols), 78 resident protocols, 29 fellow protocols, 3 intern protocols, 2 active duty student protocol, and 1 Nursing Anesthetists Course protocol. There were 148 new protocols and 1 protocol was reactivated.

There were 79 publications in nationally recognized journals. 52 presentations at regional or national medical association meetings.

### 4. Fellowship/Residency Program Support

**Fellowship/Residency programs supported by DCI:** 17 residencies and 5 fellowships, they are : *Residencies:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Podiatry, Preventive Medicine (Public Health), Radiology, Transitional Year, Urology. *Fellowships:* Developmental Pediatrics, Faculty Development (Family Practice), Geriatrics, Maternal-Fetal Medicine

134 protocols involving 118 residents

154 protocols involving 33 fellows

### 5. Other training programs supported by DCI:

Training protocols:	Department of Surgery: 3
	Department of Emergency Medicine: 2
	Department of Clinical Investigation: 2
	Department of OB/GYN: 1
	Special Forces: 2
	62nd Medical Group: 1

### 6. Other protocols supported:

1 USDA protocol

## Committee Members

Commander  
Madigan Army Medical Center  
BG GEORGE J. BROWN, M.D., MC

### Clinical Investigation Committee

Chairman  
Chief, Clinical Investigation  
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Pediatrics  
Department of OB/GYN  
Department of Family Practice  
Department of Emergency Medicine  
Department of Nursing  
Department of Medicine  
Department of Surgery  
Department of Pathology  
Department of Radiology  
Pharmacy Service  
Physical Medicine & Rehabilitation Service  
Surgical Research Service, DCI  
Clinical Studies Service, DCI  
Microbiology Service, DCI  
Biochemistry Service, DCI  
Bioresearch Service, DCI  
Research Support Service, DCI  
Lab Animal and Surgery Service, DCI  
Medical Statistician, DCI

## Committee Members (cont'd)

### Human Use Committee

Chairman  
Chief, Clinical Investigation  
COL Dan C. Moore, M.D., MC

Chief or delegated representative of:

Department of Nursing  
Department of OB/GYN  
Department of Radiology  
Department of Ministry and Pastoral Care  
Pharmacy Service  
Social Work Service  
Center Judge Advocate  
Non-institutional Member  
Surgical Research Service, DCI

### Animal Use Committee

Chairman  
Chief, Surgical Research Service, DCI  
LTC Richard Sherman, MS

Chief or delegated representative of:

Department of Clinical Investigation  
Lab Animal & Surgery Service  
Department of Nursing  
Northwest Veterinary Support Service Area  
Non-institutional Member  
NCOIC, Lab Animal & Surgery Service, DCI

## Bryon L. Steger Research Award

This award is given to residents, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1997:

*Does Insertion of a Cortical Bone Screw into Bone Change its Torsional Strength? A Biomechanical Study* by CPT George K. Bal, MC, Orthopedic Surgery Service, Department of Surgery.

Other nominees were:

*Intracavernous Drug-induced Erection Therapy versus External Vacuum Devices in the Treatment of Erectile Dysfunction*

*The Association Between Telomerase, p53 and Clinical Staging in Colorectal*

*Microencapsulated Recombinant Human Transforming Growth Factor-B1 Delivered via an Absorbable Suture Enhances Wound Healing in a Rat Incisional Wound Model*

*The Etiology of Refractive Changes at High Altitude Following Radial Keratotomy: Hypoxia Versus Hypobaria*

*Telomerase Activity in Solid Transitional Cell Carcinoma, Bladder Washings and Voided Urine*

*Evaluation of the Efficacy of Postoperative Antibiotics after Orthognathic Surgery: A Pilot Study*

*A Randomized Trial Comparing Three Methods of Bowel Preparation for Flexible Sigmoidoscopy*

*pH Paper is not an Acceptable Alternative to the Blood Gas Analyzer for Determining Pleural Fluid pH*

*A Comparison of Intermittent Pneumatic Compression of the Calf and Whole Leg in Preventing Deep Venous Thrombosis in Urological Surgery*

*Large Diameter Suction Tubing Significantly Improves Evacuation Time of Simulated Vomitus*

*The Anterior-T Frame External Fixator: A Treatment Option for High Energy Tibia Fractures*

## Fellow's Research Award

This award is given to fellows, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1997:

*Fetoplacental Vascular Tone During Fetal Circuit Acidosis, and Acidosis with Hypoxia, in the ex vivo Perfused Human Placental Cotyledon* by MAJ Nathan J. Hoeldtke, MC, Maternal Fetal Medicine, Department of OB/GYN.

Other nominees were:

*Characteristics of Outstanding Teachers of Primary Care Medicine in the United States Military*

*Unintended Pregnancy Among Female Soldiers Presenting for Prenatal Care at Madigan Army Medical Center*

*ST Segment Depression in Localizing Myocardial Ischemia in Unstable Angina*

*Impact of Aorto-coronary Graft Markers on Subsequent Graft Patency: A Retrospective Review*

## Joyce Award

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1997:

*Detection of Telomerase from Intra-Erythrocytic Stages of Plasmodium falciparum* by CPT Wade Aldous, MC, Department of Clinical Investigation.

**PUBLICATIONS**

FISCAL YEAR 97

---

**DEPARTMENT OF CLINICAL INVESTIGATION**

- |   |   |
|---|---|
| Aldous WK, Grabill NR                                     | A Fluorescent Method for Detection of Telomerase Activity. Diagnostic Molecular Pathology 6(2): 102-110, 1997.  |
| Moore KH, Bertram KA,<br>Gomez RR, Styner MJ,<br>Matej LA | Sex Hormone Binding Globulin mRNA in Human Breast Cancer: Detection in Cell Lines and Tumor Samples. J Steroid Biochem Molec Biol 59(3): 297-304, 1996.                                   |
| Sherman RA  | Short-term Stability and Habituation of Human Finger Blood-flow. Biofeedback.   |
| Sherman RA, Hill C,<br>Wong M                             | Variability in Multiple Ambulatory EMG Recordings of Pain-free Subjects. Biofeedback & Self-Regulation 21: 378, 1996.   |
| Sherman RA, Robson L,<br>Marden LA                        | The Effect of Pulsed Electromagnetic Fields on Classic Migraine Headaches. Biofeedback & Self-Regulation 21: 369, 1996.   |
| Sherman RA, Woerman<br>AL, Karstetter KW                  | Comparative Effectiveness of Videothermography, Contact Thermography, and Infrared Beam Thermography for Scanning Relative Skin Temperature. J Rehabilitation R & D 33(4): 377-386, 1996. |
- 

**DEPARTMENT OF DENTISTRY**

- |   |   |
|---|---|
| Bandrowsky T, Vorono<br>AA, Borris TJ,<br>Marcantoni HW | Amoxicillin-related Postextraction Bleeding in an Anticoagulated Patient with Tranexamic Acid Rinses. OS OM OP OR & Endodontics 82(6): 610-612, 1996. |
| Borris TJ, Bandrowsky<br>T, Vorono AA                   | Vestibuloplasty With a Split Thickness Skin Graft in a Patient with Ehlers-Danlos Syndrome. J Oral & Maxillofacial Surgery 55(4): 419-423, 1997.      |
- 

**DEPARTMENT OF EMERGENCY MEDICINE**

- |                      |   |
|----------------------|---|
| Drotts DL, Vinson DR | Incidence of Intravenous Prochlorperazine-Induced Akathisia.  |
| Pace SA, Burke TF    | Intravenous Morphine for Early Pain Relief in Patients with Acute Abdominal Pain. Academic Emergency Medicine 3(12): 1086-1092, 1996. |

### DEPARTMENT OF FAMILY PRACTICE

- Boam WD, Miser WF, Yuill SC, Delaplain CB, Gayle EL, MacDonald DC  
Comparison of Ultrasound Examination with Bone Scintiscan in the Diagnosis of Stress Fractures. JABFP 9(6): 414-417, 1996.
- Harris MD, Johnson B, Miser WF, Patience TH  
Medical Reference Databases Used by Army Primary Care Physicians in Field Environments. Military Medicine.
- Miser WF  
Topical Treatment of Chronic Anal Fissures. J Family Practice 44(4): 338, 1997.
- Scott PT, Clark JB, Miser WF  
Pertussis: An Update on Primary Prevention and Outbreak Control (Review). Amer Family Physician 56(4): 1121-1128, 1997.
- 

### MADIGAN CANCER INSTITUTE

- Daniels JL, Holt CP, Toft CK  
Genetic Counseling and Testing for Inherited Breast Cancer.
- Holt CP, Babu SS, Smith DV, Carter PL, Wilson SS, Scheffler B, Decker LA, Toft CK  
Breast Cancer Clinical Practice Pathway, Model for DOD Research and Military Medical Centers.
- Kao CC, Rand RP, Holt CP, Pierce RH, Timmons JH, Wood DE  
Internal Mammary Silicone Lymphadenopathy Mimicking Recurrent Breast Cancer. Plastic & Reconstructive Surg 99(1): 225-229, 1997.
- 

### DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE

- Eisenhauer MD, Collier HE, Eisenhauer TL, Cambier PA  
Beneficial Impact of Aorto-Coronary Graft Markers on Post-operative Angiography. Catheter & Cardiovasc Diag 40(3): 249-254, 1997.
- 

### DEPARTMENT OF MEDICINE, ENDOCRINOLOGY SERVICE

- Chapin BL, LeMar HJ, Knodel DH, Carter PL  
Secondary Hyperparathyroidism Following Biliopancreatic Diversion. Archives of Surgery 131(10): 1048-1052, 1996.
- Jones RE  
Synthesis of Ether Lipids and Phosphatidylethanolamine by Ejaculated Human Spermatozoa. Archives of Andrology 38(3): 181-189, 1997.
- 

### DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

- Anderson RH, Sy FS, Thompson S, Addy C  
Cigarette Smoking and Tuberculin Skin Test Conversion Among Incarcerated Adults. Amer J of Preventive Medicine 13(3): 175-181, 1997.

Jackson JL	The German Health System: Lessons for Reform in the United States. Arch Intern Med 157(2): 155-160, 1997.
Jackson JL, Gibbons RV, Meyer G, Inouye L	The Effect of Treating Herpes Zoster with Oral Acyclovir in Preventing Postherpetic Neuralgia. Arch Intern Med 157(8): 909-912, 1997.
Jackson JL, Kroenke K	Patient Satisfaction and Quality of Care. Military Medicine 162(4): 273-277, 1997.
Osgard EM, Jackson JL, Strong JS	A Randomized Trial Comparing Three Methods of Bowel Preparation for Flexible Sigmoidoscopy.

### DEPARTMENT OF MEDICINE, NEUROLOGY SERVICE

Elliott MA, Peroutka SJ, May EF	Reply to Athwal & Lennox Letter. Annals of Neurology 40(5): 821, 1996.
Newmark J	Thoracic Outlet Syndromes: a Non-surgeon's Perspective for Those Caring for Musicians. WORK 0(7): 95-107, 1996.

### DEPARTMENT OF MEDICINE, PULMONARY SERVICE

Grathwohl KWA, Gibbons RV, Dillard TA, Horwhat JD, Roth BJ, Thompson JW, Cambier PA	Bedside Videoscopic Placement of Feeding Tubes: Development of Fiberoptics Through the Tube. Crit Care Med 25(4): 629-634, 1997.
Roth BJ, Meyer CA	Coronary Artery Calcification at CT as a Predictor for Cardiac Complications of Thoracic Surgery. J Comput Assist Tomography 21(4): 619-622, 1997.

### DEPARTMENT OF NURSING

Jennings BLM, Staggers M	Hazards of Outcomes Management. J Outcomes Management 4(1): 18-23, 1997.
Jones RJ, Jennings BLM, Moritz P, Moss MT	Policy Issues Associated with Analyzing Outcomes of Care. Image 29(3): 261-267, 1997.
Kennedy TE, Hill E, Adams NR, Jennings BLM	A Conceptual Model of Army Nursing Practice. Nursing Management 27(10): 33-36, 1996.

### DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Brown Z, Selke S, Zeh J, Kopelman JN, Maslow AS, Corey L, Watts H, Berry S	The Acquisition of Herpes Simplex Virus During Pregnancy. NEJM 337: 509-515, 1997.
--	--



## PUBLICATIONS - MAMC - FY 97

- |  |   |
|--|---|
| DeQuattro N, Hibbert ML, Buller JL, Russell CS, Neill GF, Poore SE, Davis GD | Minilaparoscopic Tubal Ligation Under Local Anesthesia. J Am Assoc Gynecol Laparosc 4(4): S22, 1997.                                      |
| Hibbert ML, Buller JL, Seymour SD, Poore SE, Davis GD                        | A Minilaparoscopic Technique for Pomeroy Tubal Ligation. Obstet & Gynecol 90(2): 249-251, 1997.   |
| Hibbert ML, Kambiss SM, Palacia PE, Davis GD, Perez RP                       | Lost Needle During Operative Laparoscopy: The Use of the Minilaparoscope in its Discovery and Retrieval. J Pelv Surg 3(5): 265-267, 1997. |
- 

## DEPARTMENT OF PEDIATRICS

- |   |  |
|---|--|
| Carter ER   | It Is Time to Consider Standardizing the Interrupter Technique (Correspondence to the Editor). Eur Respir J 10: 1428-1429, 1997.         |
| Carter ER   | Medical Meetings: A Chance for Braindusting (Letter to the Editor). CHEST 112(2): 567, 1997.   |
| Carter ER, Behrens ML, Moffitt DR                   | Nose Clips: Why Worry About Them?. Respiratory Care 42(5): 487-488, 1997.  |
| Carter ER, Webb CR, Moffitt DR                      | Evaluation of Heliox in Children Hospitalized with Acute Severe Asthma. Pediatrics (Supplement to) 100(2): 305, 1997.                    |
| Hinson RM, Miller RC, Macri CJ                      | Femoral Hypoplasia and Maternal Diabetes: Consider Femoral Hypoplasia/Unusual Facies Syndrome. Amer J Perinatology 13(7): 433-436, 1996. |
| Pina JS, Behrens ML, Moffitt DR, Roth BJ, Carter ER | Are Nose Clips Necessary in Adults and Children Performing Forced Expiratory Spirometry?. Respiratory Care 42(5): 492-497, 1997.         |
- 

## PHARMACY SERVICE

- |                      |   |
|----------------------|---|
| Rembold JM, Berry TR | Initial Success and Substantial Government Savings May Mandate Prime Vendor Contracts for Table of Organization and Equipment Units and Development Support. Military Medicine 162(1): 68-70, 1997. |
|----------------------|---|
- 

## PHYSICAL MEDICINE & REHABILITATION SERVICE

- |   |  |
|---|--|
| Divelbiss BJ, Kumar SJ                                    | Isolated Traumatic Denervation of the Extensor Pollicis Longus. Arch Phys Med & Rehabilitation 78(7): 783-785, 1997. |
| Lauder TD, Williams MV, Campbell CS, Davis GD, Sherman RA | Abnormal Eating Behavior in Military Women. Med Sci Sports Exercise.   |

---

**DEPARTMENT OF RADIOLOGY**

- Bender GN Radiographic Examination of the Small Bowel; An Application of Odds Ratio Analysis to Help Attain an Appropriate Mix of Small Bowel Follow Through and Enteroclysis in a Working-Clinical Environment. Investigative Radiology 32(6): 357-362, 1997.
- Bender GN, Hunter GJ, Tsuchida AM, Timmons JH Fluoroscopic Decompression of the Acutely Dilated Colon: Indications and Technique. Emergency Radiology 4(4): 225-235, 1997.
- Bender GN, Makuch RS Double-contrast Barium Examination of the Upper Gastrointestinal Tract with Nonendoscopic Biopsy: Findings in 100 Patients. Radiology 202(2): 355-359, 1997.
- Makuch RS, Bender GN, Brisette MD, Tsuchida AM Fluoroscopic-Guided in Vivo Gastric Mapping for Assessment of Gastric Carcinoma (Case Report). Investigative Radiology 32(8): 496-499, 1997.
- Mansfield LT, Youngberg RA Intraarticular Ganglia of the Knee: Prevalence, Presentation, Etiology, and Management. Amer J Radiology 168(1): 123-127, 1997.
- Mansfield LT, Youngberg RA MR Orthogonal Views of the Femoral Neck: Oblique-Axial View from the Oblique-Coronal Plane. JCAT 21(2): 299-301, 1997.
- Mansfield LT, Youngberg RA, Warne WJ, Pitcher JD, Nguyen PL Potential Cost Savings of MR Imaging Obtained before Arthroscopy of the Knee: Evaluation of 50 Consecutive Patients. Amer J Roentgenology 168(4): 913-918, 1997.
- Meyer CA, Pina JS, Taillon D, Godwin JD Inspiratory and Expiratory High-resolution CT Findings in a Patient with Sjogren's Syndrome and Cystic Lung Disease. Amer J Roentgenology 168(1): 101-103, 1997.
- Walsh DW, Ho VB, Haggerty MF Mycotic Aneurysm of the Aorta: MRI and MRA Features. JMRI 7(2): 312-315, 1997.
- Williams JB, Ho VB, Wettlaufer JN, Bush WH Gadoteridol as an Alternative Contrast Agent for Retrograde Pyelography. Abdominal Imaging 22(2): 233-234, 1997.
- Williams JB, Youngberg RA, Mansfield LT, Pitcher JD MR Imaging of Skeletal Muscle Metastases. Amer J Roentgenology 168(2): 555-557, 1997.
- Williams SC, Contreras M, McBiles M, Cawthon MA, Shah RB The Impact of a Picture Archiving and Communication System on Nuclear Medicine Examination Interpretation. Journal of Digital Imaging 10(2): 51-56, 1997.

### **SOCIAL WORK SERVICE**

- Raiha NK, Soma DJ      Victims of Child Abuse and Neglect in the U.S. Army. Child Abuse & Neglect 21(8): 759-768, 1997.
- 

### **DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE**

- Ainbinder DJ, Haik BG,      Gadolinium Enhancement: Improved MRI Detection of  
Frei DF, Gupta KL,      Retinoblastoma Extension into the Optic Nerve.  
Mafee MF      Neuroradiology 38(8): 778-781, 1996.
- Ainbinder DJ, Mazzoli      The Posttherapeutic Orbit IN: "Posttherapeutic  
RA, Mafee MF, Huchun      Neurodiagnostic Imaging", Chapter IIA, J.R. Jenkins (Ed),  
A, Haik BG      Lippincott-Raven, New York: 39-68, 1997.
- George RK, Chan CC,      Ocular Immunopathology of Behcet's Disease (Review).  
Whitcup SM,      Survey of Ophthalmology 42(2): 157-162, 1997.  
Nussenblatt RB
- Mader TH      Bilateral Photorefractive Keratectomy with Intentional  
Unilateral Undercorrection Performed on an Aircraft Pilot. J  
Cataract Refract Surg 23: 145-147, 1997.
- May EF, Truxal AR      Loss of Vision Alone May Result in Seesaw Nystagmus  
(Review). J Neuro-Ophthalmology 17(2): 84-85, 1997.
- White LJ, Mader TH      Effects of Hypoxia and High Altitude Following Refractive  
Surgery. Ophthalmic Practice 15(5): 1997.
- 

### **DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE**

- DeVine JH, Rooney RC,      Dysplasia Epiphysealis Hemimelica in an Elderly Patient.  
Carpenter CT, Pitcher      Amer J Orthopedics 26(3): 223-225, 1997.  
JD
- 

### **DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE**

- Perkins JA, Sie KC,      Airway Management in Children with Craniofacial  
Milczuk H, Richardson      Anomalies. Cleft Palate-Craniofacial J 34(2): 135-140, 1997.  
MA
- Ruegemer JL, Perkins      The Effect of the Palmaz Balloon Expandable Metallic Stent  
JA, Thomas RW,      in the Trachea of Pigs. Otolaryngology H & N Surgery.  
O'Bryant LK, Nielsen  
RE, Azarow KS
- 

### **DEPARTMENT OF SURGERY, UROLOGY SERVICE**

- Berry DL, Moinpour      Measurement of Irritative Bladder Symptoms. Onc Nurs  
CM, Blumenstein BA,      Forum 24: 319, 1997.  
Thrasher JB, Ellis WJ

- |  |   |
|--|---|
| Peterson AC, Ruiz HE,<br>Soderdahl DW                                    | Non-Hodgkin's Lymphoma with Bladder Involvement. Urology 50(3): 444-445, 1997.  |
| Soderdahl DW,<br>Henderson SR,<br>Hansberry KL                           | A Comparison of Intermittent Pneumatic Compression of the Calf and Whole Leg in Preventing Deep Venous Thrombosis in Urological Surgery. J of Urology 157: 1774-1776, 1997.                               |
| Soderdahl DW, Knight<br>RW, Hansberry KL                                 | Erectile Dysfunction Following Transurethral Resection of the Prostate. Journal of Urology 156(4): 1354-1356, 1996.   |
| Soderdahl DW, Petroski<br>RA, Mode D, Schwartz<br>BF, Thrasher JB        | The Use of an External Vacuum Device to Augment a Penile Prosthesis. Techniques in Urology 3(2): 100-102, 1997.   |
| Soderdahl DW,<br>Thrasher JB   | A Novel Technique to Prevent Foley Catheter Loss Following Radical Retropubic Prostatectomy. Techniques in Urology 3(2): 69-71, 1997.   |
| Soderdahl DW,<br>Thrasher JB,<br>Hansberry KL                            | Bilateral Renal Cell Carcinoma in Autosomal Dominant Polycystic Kidney Disease, A Case Report and Literature Review. Am J Nephrol 17(1): 96-99, 97.   |
| Soderdahl DW,<br>Thrasher JB,<br>Hansberry KL                            | Intracavernosal Drug-induced Erection Therapy Versus External Vacuum Devices in the Treatment of Erectile Dysfunction. British J of Urology 79(6): 952-957, 1997.   |
| Soderdahl DW,<br>Wettlaufer JN, Corn B,<br>Gomella LG                    | Neoadjuvant Hormonal Therapy in the Management of Prostate Cancer: A Surgical and Radiation Therapy Review. Techniques in Urology 2(4): 194-206, 1996.  |
| Thrasher JB, Kao TC,<br>Garner D, Mooneyham<br>RD, Cruess DF, Moul<br>JW | Multicenter Patient Self-reported Questionnaire (PSQ) of Incontinence (IN), Impotence (IM), Stricture (S), and Quality of Life (QOL) after Radical Prostatectomy (RP). J of Urology 155(647): 1345, 1996. |

## PRESENTATIONS

FISCAL YEAR 97

---

### DEPARTMENT OF CLINICAL INVESTIGATION

Aldous WK, Keene CA, Shook ME, Brown TA	Quantification of Telomerase in Human Tissues.	Society of Armed Forces Medical Laboratory Scientists, Spokane, USA, March 97.
Aldous WK, Niemeyer DM, Gower WR, Moore KH, Karge W	An Introduction to Molecular Biology.	SAFMLS Annual Meeting, Spokane, USA, March 97.
Heath GW	Introduction of <i>Fundulus gardneri</i> as a Bioassay Model for Carcinogenicity and Toxicological Testing.	American Association of Laboratory Animal Science, Montana Branch, MT, March 97.
Hill C, Sherman RA, Wong M	Variability in Multiple Ambulatory EMG Recordings of Pain-free Subjects.	Association Applied Psychophysiology, Albuquerque, USA, March 97.
Moore KH, Matej LA, Styner MJ	Characterization of Sex Hormone Binding-Globulin (SHBG) in Breast and Prostate Cancer.	Society of Armed Forces Medical Laboratory Scientists, Spokane, USA, March 97.
Qabar AN, Bullock JM, Matej LA	A Chimeric Murine TSP3/Human TSP1 is a Pentamer with Abolished Antiangiogenic Activity.	FASEB '97, New Orleans, USA, April 97.
Sherman RA, Marden LA, Robson L	Treatment of Headaches with Pulsing Electromagnetic Fields.	International Association for Study of Pain, Vancouver, Canada, August 97.
Sherman RA, Robson L, Marden LA	Treatment of Aura-Inaugurated Migraine Headache (Classic Migraine) with Pulsing Electromagnetic Fields[colon] A Pilot Efficacy Study.	International Association for Study of Pain, Vancouver, Canada, August 97.

---

### DEPARTMENT OF EMERGENCY MEDICINE

Pace SA	Comparison of the 12-Lead Electrocardiogram to Detect Acute MI or Unstable Angina in Patients with and without Ongoing Chest Pain.	Society for Academic Emergency Medicine Annual Meeting, Washington, USA, May 97.
Pace SA	Are Typical Coronary Risk Factors Associated with Acute MI or Unstable Angina in ED Patients with Chest Pain.	Society for Academic Emergency Medicine Annual Meeting, Washington, USA, May 97.

### DEPARTMENT OF FAMILY PRACTICE

Harrington BC, Meier CM, Crouch DN, Kugler JP, Edmonds DJ, Patience TH	Maternal Heart Rate and Blood Pressure to Exercise in Early Pregnancy as a Predictor of Preeclampsia.	48th Annual AAFP Scientific Assembly of American Academy of Family Physicians, New Orleans, USA, October 96.
Miser WF, Evans P	Teaching the Professional Boundaries in the Physician-Patient Relationship.	STFM Annual Spring Conference, Boston, USA, May 97.

### MADIGAN CANCER INSTITUTE

Daniels JL, Holt CP, Toft CK	Genetic Counseling and Testing for Inherited Breast Cancer.	Genetics Symposium, Tacoma, USA, August 97.
Holt CP, Babu SS, Smith DV, Carter PL, Wilson SS, Scheffler B, Decker LA, Toft CK	Breast Cancer Clinical Practice Pathway, Model for DOD Research and Military Medical Centers.	DOD Breast Cancer Conference, Washington, USA, July 97.

### DEPARTMENT OF MEDICINE, INTERNAL MEDICINE SERVICE

Jackson JL, Otlege J, Sneiden S	Results of the Semmes-Weinstein Monofilament Trial.	Society of General Internal Medicine National Meeting, Washington, USA, May 97.
Osgard EM, Jackson JL, Strong JS	A Randomized Trial Comparing Three Methods of Bowel Preparation for Flexible Sigmoidoscopy.	American College of Physicians, Philadelphia, USA, March 97.
Woolman BA, Barker AJ, Barrett JP	Treatment of Leg Muscle Cramps[colon] A Double-blind Placebo-controlled Crossover Trial of Magnesium Oxide.	Faculty Development Fellowship Program, UW, Dept Family Medicine, Seattle, USA, May 97.

---

**DEPARTMENT OF MEDICINE, CARDIOLOGY SERVICE**

LeClerc KM, Cambier PA, Mascette AM	The Effect of Left Ventricular Hypertrophy on Diastolic Function at Rest and After Exercise.	Army ACP, October 96.
---	--	-----------------------

---

**DEPARTMENT OF MEDICINE, PULMONARY SERVICE**

Murray TR, Thompson JW, Roth BJ	Long Term Effect of Therapeutic Lung Radiation on Exercise.	Chest Conference, San Francisco, USA, October 96.
---------------------------------------	--	---

---

**DEPARTMENT OF NURSING**

Chapman JB, Hunter BP, Armondo AA	Effect of Prophylactic Preoperative Intravenous Caffeine Administration on the Incidence of Postoperative Headache in the Daily Caffeine User.	American Association of Nurse Anesthetists National Meeting, San Francisco, USA, August 97.
---	--	--

DePaul D, Renaud MT, Phyll G, Loan LA	Fatigue Following Childbirth[colon] Military Family Outcomes.	Celebrating Nursing Research Scholarship, PLU, Tacoma, USA, May 97.
---	--	--

DePaul D, Renaud MT, Phyll G, Loan LA	Fatigue Following Childbirth[colon] Military Family Outcomes.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
---	--	--

Jennings BLM, Anderson FD, Loan LA, Wilson SK	A Survey to Access to Care in the TRICARE Environment.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
--	---	--

Loan LA	Neonatal Implications of Ventilator Inspired Gas Temperatures.	Sigma Theta Tau International Nursing Research Congress, Vancouver, Canada, June 97.
---------	---	--

Loan LA, Jennings BLM	A Description of Patient Satisfaction and Loyalty in Military Beneficiaries Choosing to Change TRICARE Prime Managed Care Option.	American Association of Ambulatory Care Nurses National Meeting, Seattle, USA, March 97.
--------------------------	---	---

McCarthy MS, Clark SJ, Roth BJ, Grathwohl KWA	Gastric/Jejunal Feeding[colon] Nutritional Outcomes and Pneumonia.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
---	--	--

## PRESENTATIONS - MAMC - FY 97

Moore CJ, Sweet NL, Williams EJ	Performance and Skill Retention of Anesthesia Providers Using the Field Anesthesia Machine.	American Association of Nurse Anesthetists National Meeting, San Francisco, USA, August 97.
Peniston J, Wilson SK, Lombardi W	Wellness Intervention with Pregnant Soldiers.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
Renaud MT, DePaul D	Fatigue Following Childbirth[colon] Military Family Outcomes.	AWHONN National Conference, Washington, USA, June 97.
Renaud MT, Depaul D	Neonatal Outcomes in a Modified NICU Environment.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
Schempp CM	Soldier HIV Behavior Modification.	American Association of Ambulatory Care Nurses National Meeting, Seattle, USA, March 97.
Schempp CM	Soldier HIV Behavior Modification.	TriService Nursing Research Dissemination Conference, Bethesda, USA, August 97.
Wilson SK, Birgenheier PS	Impact of a Research Project on Clinical Practice[colon] Year Three Evaluation.	Alternative/Complimentary Modalities in Nursing Practice, Anchorage, USA, May 97.
Wilson SK, Birgenheier PS	Impact of a Research Project on Clinical Practice[colon] Year Three Evaluation.	Theta Omicron Chapter of Sigma Theta Tau Conference, Anchorage, USA, September 97.

---

## DEPARTMENT OF OBSTETRICS/GYNECOLOGY

Markenson GR	The Use of the Polymerase Chain Reaction to Detect Bacteria in Amniotic Fluid in Pregnancies Complicated by Preterm Labor.	17th Annual Society of Perinatal Obstetricians, Anaheim, USA, January 97.
Wong M, Davis GD, Sherman RA	Ambulatory Recording of Urodynamic Functioning in Female Soldiers During Training.	Association for Applied Psychophysiology and Biofeedback, San Diego, USA, March 97.



### **PREVENTIVE MEDICINE SERVICE**

Kortepeter M, Krauss MR, Gunzenhauser JD	Risk Factors for Heavy Alcohol Use in an Active Duty Population at Ft Lewis.	Prevention 97, 14th Annual National Preventive Medicine Meeting, Atlanta, USA, March 97.
Krauss MR, Goldman DP	Seroprevalence of Cryptosporidium Among Active Duty Soldiers.	Prevention 97, 14th Annual National Preventive Medicine Meeting, Atlanta, USA, March 97.
Niebuhr DW, Krauss MR, Gunzenhauser J, Siscovick DS, Schwartz SM	Risk of Myocardial Infarction Associated with Physical Inactivity in Young Women.	Prevention 97, 14th Annual National Preventive Medicine Meeting, Atlanta, USA, March 97.
Rumm PD, Krauss MR, Rivara F, Bell M	Spouse and Child Abuse in a Military Population.	Prevention 97, 14th Annual National Preventive Medicine Meeting, Atlanta, USA, March 97.

---

### **DEPARTMENT OF PEDIATRICS**

Gries DM, Barfield WA, Phyll G	Evaluation of an Early Discharge Program of Mothers and Infants Following Childbirth in a Military Population.	Uniformed Services Pediatric Seminar, San Antonio, USA, March 97.
--------------------------------------	---	---

---

### **PHYSICAL MEDICINE & REHABILITATION SERVICE**

Lauder TD, Williams MV, Campbell CS, Davis GD, Sherman RA	Abnormal Eating Behaviors in Military Women.	American College of Sports Medicine, Denver, USA, May 97.
---	---	---

---

### **DEPARTMENT OF RADIOLOGY**

Casha LM, Kransdorf MJ, Youngberg RA	Benign and Malignant Soft Tissue Tumors. Do Certain Tumors Tend to Occur in Certain Locations and are Certain Tumors More Common in certain Ages.	AMED Conference, February 97.
Makuch RS, Bender GN	Non-Endoscopic Gastric Biopsy Program in Support of the Double Contrast Upper Gastrointestinal Examination.	82nd Annual Meeting of Radiological Society of North America, Chicago, USA, December 96.

Makuch RS, Bender GN	Proximal Small Bowel Biopsy Before Enteroclysis.	82nd Annual Meeting of Radiological Society of North American, Chicago, USA, December 96.
Mansfield LT, Youngberg RA, Pitcher JD	Intravenous Contrast Enhanced MR Saline Arthrography[colon] A Technique for Staging Juxta- Articular Masses.	Current Concepts in Imaging, Coronado, USA, February 97.
Varma MK, Youngberg RA, Mansfield LT, Pitcher JD	Radiologic Guided Aspiration of Intra-Articular Ganglia in the Knee.	AMEDD Radiology Conference, San Diego, USA, February 97.
Walsh DW, Bender GN	Comparison of CT-Enteroclysis and Traditional CT in the Setting of Suspected partial Small Bowel Obstruction.	Current Concepts in Imaging, San Diego, USA, February 97.
Whitaker MA, Morissette JC, Hanny L	Construction of a Computer-Based Generic Breast Model to Test the Validity of the Nipple Distance Abnormality Localization Method.	Current Concepts in Imaging, Coronado, USA, February 97.

---

**DEPARTMENT OF SURGERY, ORTHOPEDICS SERVICE**

Bal GK, Benirschke SK, Henley MB, Tencer A	Does Insertion of a Cortical Bone Screw Into Bone Change the Torsional Strength?.	North Pacific Orthopedic Society 1997 Annual Meeting
Bal GK, Chapman JR, Henley MB, Benirschke SK, Claudi B	The Anterior T-Frame External Fixator, A Treatment Option for High Energy Proximal Tibia Injuries.	AOA Residents Course, New York, USA, March 97.
Bal GK, Henley MB, Benirschke SK, Tencer A	Does Insertion of a Bone Screw Alter Its Torsional Strength? A Biomechanical Study.	AOA Residents Course, New York, USA, March 97.

---

**DEPARTMENT OF SURGERY, GENERAL SURGERY SERVICE**

Jorden TV, Dyster M, McLean D	A Primary Care Physician's Experience with PSA Testing.	James C. Kimbrough Urological Seminar, Scottsdale, USA, December 96.
Peterson AC, Lance RS, Ruiz HE	Outcomes and Recurrence of Varicocele Ligation Done for Pain.	AUA, Western Section, Salt Lake City, USA, September 97.

## DEPARTMENT OF SURGERY, OPHTHALMOLOGY SERVICE

Chun BB, Mader TH, Nelson ML, Raymond WR, Hansen EA, Mazzoli RA	Pericardium and Fascia Lata[colon] Comparison of Physical Characteristics.	Association for Research in Vision and Ophthalmology, Ft Lauderdale, USA, May 97.
Mader TH, Blanton CL, Gilbert BN, Kubis KC, Schalhorn SC, White LJ, Parmley VC, Ng JD	Refractive Changes During 72-hour Exposure to High Altitude After Refractive Surgery.	American Academy of Ophthalmology, Centennial Annual Meeting, Chicago, USA, October 96.
May EF, Coughlin WF, Stankus SJ, Jones KW, Peroutka SJ	Autosomal Dominant Vertical and Horizontal Nystagmus[colon] A Vestibulocerebellar Syndrome That Does Not Map to Chromosome.	American Academy of Neurology, Boston, USA, April 97.
Mazzoli RA, Mader TH, Parmley VC, Ho VB, Rovira MJ, Coughlin WF, George DP	Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by MR and CT Imaging in the Goat.	Annual Scientific Symposium, WA Academy of Eye Physicians & Surgeons, Yakima, USA, September 97.
Nelson ML, Raymond WR, Wroblewski KJ, Chun BB, Stephan MJ, Mazzoli RA, Hansen EA	Ocular Findings in Robinow (Fetal Face) Syndrome.	Association for Research in Vision and Ophthalmology, Ft Lauderdale, USA, May 97.
Torres MF	Intracranial Hypertension Associated with Minocycline.	North American Neuro- Ophthalmology Society Meeting, Keystone, USA, February 97.
Torres MF	The Contribution of the Donor Cornea to Final Corneal Curvature in Penetrating Keratoplasty.	Association for Research in Vision and Ophthalmology Conference, Ft Lauderdale, USA, May 97.
Torres MF, Mazzoli RA, Hansen EA, Ng JD, Raymond WR	Combined Porous Implant and Thin Dermis Fat Graft for Complex Socket Reconstruction.	American Academy of Ophthalmology, Centennial Annual Meeting, Chicago, USA, October 96.

Winkle RA, Chismire KJ, Dahlhauser KF, Lauder TD	Weight Lifting with and without Valsalva and Intraocular Pressure.	Association for Research in Vision and Ophthalmology Conference, Ft Lauderdale, USA, May 97.
Winkle RA, Mader TH, Parmley VC, White LJ, Polse KA	The Etiology of Refractive Changes at High Altitude Following Radial Keratotomy[colon] Hypoxia Versus Hypobaria.	American Academy of Ophthalmology, Centennial Annual Meeting, Chicago, USA, October 96.
Wroblewski KJ, Dahlhauser KF, Mader TH	Anterior Capsular Contraction with Foldable Silicone Intraocular Lenses.	American Academy of Ophthalmology, Chicago, USA, October 96.
Wroblewski KJ, Mader TH, Parmley VC, Torres MF	Long Term Graft Survival in Down's Patients After Penetrating Keratoplasty.	Association for Research in Vision and Ophthalmology Conference, Ft Lauderdale, USA, May 97.
Wroblewski KJ, May EF, Grazko MB, Patience TH	Pulfrich's Phenomenon in Patients with Optic Neuropathy.	North American Neuro- Ophthalmology Society, Keystone, USA, February 97.
Wroblewski KJ, May EF, Grazko MB, Pulos E	Utility and Validity of Pulfrich's Phenomenon.	North American Neuro- Ophthalmology Society Meeting, Keystone, USA, February 97.

#### DEPARTMENT OF SURGERY, OTOLARYNGOLOGY SERVICE

Kanne TJ, Perkins JA	Newborn Hearing Screening with Otoacoustic Emissions at Madigan Army Medical Center.	Annual Combined Otolaryngological Spring Meeting, Scottsdale, USA, May 97.
Mesaros GJ, Martin RK, Edmond CV, Waldner DT	The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas.	Gary Wratten Surgical Symposium, San Diego, USA, April 97.
Ruegemer JL, Perkins JA, Thomas RW, O'Bryant LK, Nielsen RE, Azarow KS	The Effect of the Palmaz Expandable Metallic Stent in the Trachea of Pigs.	American Academy of Otolaryngology-Head and Neck Surgery, Annual Meeting, San Francisco, USA, September 97.
Song AU	Success of Preoperative Imaging & Unilateral Neck Exploration for Primary Hyperparathyroidism.	American Academy of Otolaryngology-Head and Neck Surgery, Annual Meeting, San Francisco, USA, September 97.

## PRESENTATIONS - MAMC - FY 97

Song AU	NM23 "Antimetastatic" Gene Product Expression in Head and Neck Squamous Cell Carcinoma.	American Academy of Otolaryngology-Head and Neck Surgery, Annual Meeting, San Francisco, USA, September 97.
Ulnick KM	Madigan's Experience with Obstructive Sleep Apnea.	Multi-disciplinary Approach to Obstructive Sleep Apnea, Surgeon General, Tacoma, USA, August 97.

---

## DEPARTMENT OF SURGERY, UROLOGY SERVICE

Berry DL, Moinpour CM, Blumenstein BA, Thrasher JB, Ellis WJ	Measurement of Irritative Bladder Symptoms.	Oncology Nursing Society Annual Congress, New Orleans, USA, May 97.
Feber KM, Ruiz HE	Vasovasostomy[colon] A Retrospective Review of Vasovasostomy Using Loupe Magnification.	James C. Kimbrough Urological Seminar, Scottsdale, USA, December 96.
Lance RS, Maddison L, Bae VL, Thrasher JB, Plymate SR	Type 1 Insulin-like Growth Factor Receptor Number Determines the Growth Potential of Androgen Insensitive Immortalized Prostate Cancer Cells.	1996 SBUR Fall Symposium, Maywood, USA, December 97.
Schwartz GH, Sudduth RH	Detection of Helicobacter Pylori Using Rapid Serological Testing in Patients with Nonulcerative Dyspepsia.	American College Physicians, Philadelphia, USA, March 97.
Soderdahl DW	Comparison of Five Second Urinary Home Flow Rates to Formal In-Office Uroflowmetry.	James C. Kimbrough Urological Seminar, Scottsdale, USA, December 96.
Soderdahl DW, Thrasher JB, Hansberry KL	Intracavernous Drug-induced Erection Therapy Versus External Vacuum Devices in the Treatment of Erectile Dysfunction.	American Urological Association, 92nd Annual Meeting, New Orleans, USA, April 97.

# INDEX TO PROTOCOLS

**O = Ongoing    T = Terminated**  
**C = Completed    S = Suspended**

PI and No.	Status	Title	Page
<b>62nd Medical Group</b>			<b>63</b>
Martinez CH #95/143	C	Training of Veterinary Food Inspection Personnel in Field Slaughter and Inspection Methods Utilizing Domestic Swine ( <i>Sus scrofa domestica</i> )	64
<b>Fort Lewis, Special Forces</b>			<b>65</b>
Taylor C #94/069	C	Special Operations Medical NCO Sustainment Training	66
Taylor C #97/117	O	Special Operations Medical NCO Sustainment Training Using the Goat Model ( <i>Capra hircus</i> )	67
<b>United States Department of Agriculture</b>			<b>68</b>
Burri BJ #92/001	O	Methods for Assessing Vitamin A Status in Healthy Adults	69
<b>Department of Anesthesia &amp; Operative Services</b>			<b>70</b>
Miller BJ #96/042	T	Prolonged Analgesia Using Microencapsulated Morphine in A Mouse Model ( <i>Mus musculus</i> )	71
<b>Department of Clinical Investigation</b>			<b>72</b>
Aldous WK #95/103	T	Polymerase Chain Reaction Detection and Cell Culture of Herpes Simplex Virus from Urine of Symptomatic Males with Non-gonococcal Urethritis	73
Aldous WK #95/025	O	The Department of Clinical Investigation's Molecular Biology Short Course for Physicians	74
Aldous WK #96/058	O	Detection of Telomerase Activity from <i>Plasmodium falciparum</i>	75
Aldous WK #96/162	C	Indirect Quantitation of Telomerase Activity	76
Heath GW #97/031	T	Introduction of <i>Fundulus gardneri</i> as A Bioassay Model for Carcinogenicity and Toxicological Testing	77
Matej LA #94/169	T	Development of a Method to Study What Proteins Are Regulated by IGF in the PC3 Prostate Cancer Cell Line Using 2-D Gel Electrophoresis and Protein Sequencing	78
McClellan DR #90/091	O	A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp(6)-Des-Gly(10)-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing....	79

PI and No.	Status	Title	Page
Moore DC #95/081	T	Genentech National Cooperative Growth Study (NCGS) Post Marketing Surveillance Program for Protropin (Somatrem for Injection) and Nutropin (Somatropin [rDHA Origin]) for Injection)	80
Moore KH #96/033	C	Localization and Identification of Sex Hormone Binding Globulin (SHBG) mRNA and SHBG-Related Proteins in Breast Cancer (Production of Monoclonal Antibodies Using Mice)	81
Moore KH #95/126	O	Sex Hormone Binding Globulin and Prostate Cancer - Characterization of Alternate mRNA Transcripts	82
Moore KH #97/033	O	Is BRCA1 Loss of Expression Found in Tumors Others Than Breast and Ovarian Cancer	83
Moore KH #97/128	O	Enhancing the Effectiveness of Tamoxifen Therapy in Breast Cancer	84
Nielsen RE #94/084	T	Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine <i>Sus scrofa</i> , Goat <i>Capra hircus</i> , Rabbit <i>Oryctolagus cuniculus</i> , Ferret <i>Mustela putorius furo</i> , Rat <i>Rattus</i> ...	85
Patience TH #93/052	T	Intrauterine Growth: Factors That Influence the Relationship Between Gestational Age and Birth Weight, Length, and Head Circumference	86
Qabar AN #97/013	O	The Role of Thrombospondin in Macrophage-Mediated Wound Healing. A Structural/Functional Dissection of Thrombospondin	87
Ramayya MS #97/118	O	Characterization, Tissue Expression, and Functional Studies of Alternate Splice Products of Human Steroidogenic Factor-1 (hSF-1)	88
Sherman RA #95/014	C	Relationships Between A Female Soldier's Military Occupational Specialty (MOS) and Birth Outcomes	89
Sherman RA #95/139	O	Pilot Study for Wound Healing Using Pulsed Electromagnetic Field Therapy	90
Sherman RA #95/153	T	Use of Pulsing Electromagnetic Fields to Potentiate Healing of Stable, Open Ulcers on the Lower Limbs and Feet	91
Sherman RA #96/126	O	Incidence and Impact of Headaches Among Users of Medical and Dental Facilities at Fort Lewis	92
Sherman RA #96/019	O	Treatment of Aura-Inaugurated Migraine Headache (Classic Migraine) with Pulsing Electromagnetic Fields: A Pilot Efficacy Study	93
Sherman RA #96/085	O	Treatment of Headaches with Pulsing Electromagnetic Fields: A Multigroup, Double-Blind, Placebo-Controlled Study	94
Sherman RA #96/151	C	Short-term Stability and Habituation of Human Finger Blood-Flow	95

PI and No.	Status	Title	Page
Sherman RA #97/109	T	Biofeedback Measures of Pelvic Floor Muscle Function in Incontinent and Asymptomatic Women	96
Sherman RA #96/131	C	Treatment of Inflammation Related Low Back Pain with Pulsing Electromagnetic Fields: A Pilot Efficacy Study	97
Sherman RA #97/058	O	Determination of whether a Pronation-Controlling Insole Reduces the Occurrence of Lower Limb Pain Among Overpronating Soldiers During Basic Training	98
Sherman RA #95/158	O	Pilot Study For: Environmental-Temporal Relationships Between Changes in (a) Paraspinal Muscle Tension and Low Back Pain and (b) Trapezius Muscle Tension and Migraine and Tension Headache Intensity	99
<b>Department of Dentistry</b>			<b>100</b>
Fiaschetti DK #97/053	O	A Survey of Sedation and General Anesthesia Techniques of the Oral and Maxillofacial Surgery Practitioner	101
Marcantoni HW #96/046	O	Evaluation of the Efficacy of Post-operative Antibiotics After Orthognathic Surgery	102
<b>Department of Emergency Medicine</b>			<b>103</b>
Brantner RD #96/014	T	Patients Who Leave A Military Hospital Emergency Department Without Being Seen by a Physician	104
Brantner RD #93/120	T	The Randomized Use of Helium-Oxygen Mixture for the Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease. A Blinded Trial	105
Burke TF #94/116	C	Multicenter, Prospective, Double-Blind Randomized Comparative Trial to Evaluate the Treatment Effects of Ciprofloxacin for 7 Days, Compared with Standard Therapy for 14 Days, In...acute Pyelonephritis	106
Charette JD #97/055	O	A Randomized, Double-Blind, Multicenter Trial Comparing 10 Days of Oral Therapy with Trovafloxacin - CP-99,219 and 14 days of Oral Clarithromycin for the Treatment of Acute Sinusitis	107
Drotts DL #97/116	O	Incidence of Intravenous Prochlorperazine-Induced Akathisia	108
Fuller F #97/062	C	Out-of-Hospital Initiated Intravenous Lines: Are We Starting Too Many?	109
Fuller F #97/020	O	A Model for Prehospital 12-Lead Acquisition Without A Dedicated 12-Lead ECG Machine	110
Hoffman JR #95/189	C	Analgesia for Reduction of Acute Glenohumeral Dislocation: Intra-articular Lidocaine Versus Intravenous Fentanyl	111
Pace SA #97/028	O	Prospective, Randomized, Double-Blind Comparison of the Safety and Efficacy of BAY 12-8039 400 MG QD x 10 Days vs 400 mg QD x 5 Days vs Clarithromycin 500 mg BID x 10 Days for the Treatment of ...	112



PI and No.	Status	Title	Page
Pace SA #96/062	C	Double-Blind, Randomized, Comparative, Multicenter Study of Zagam (Sparfloxacin) vs. Biaxin (Clarithromycin) in the Treatment of Community-Acquired Pneumonia	113
Pace SA #94/152	T	Pediatric Intubation Training Utilizing the Ferret Model	114
Pace SA #94/165	T	Emergency Surgical Procedures Laboratory Training Utilizing the Goat ( <i>Capra hircus</i> )	115
Pace SA #97/133	O	Pain Treatment and Documentation by Paramedics	116
Pace SA #97/139	O	A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter Study to Investigate the Efficacy and Safety of Inhaled Zanamivir (GG167) 10 mg Administered Twice a Day for Five Days.....	117
Vandenberg JT #97/021	C	Comparison of Currently Available Oropharyngeal Suction Systems vs. New Large Diameter System in Time to Intubation	118
Wedmore IS #97/127	O	Efficacy of Clonidine for Prophylaxis of Acute Mountain Sickness	119
<b>Department of Family Practice</b>			<b>120</b>
Benson PJ #97/018	C	Biomechanics of the A2 Flexor Tendon Pulley in A Climbing Position Cadaver Model: Effects of Circumferential Taping	121
Chun YH #96/127	O	Incidence of Exercise Induced Hematuria After the Army Physical Fitness Test (APFT)	122
Clark JB #96/056	C	Incidence of Unintended Pregnancy in Female Soldiers Presenting to OB Orientation at Madigan Army Medical Center From March 1996 to February 1997	123
Dombroski RT #97/022	T	Healing of Stress Fractures and Shin Splints Using Non-thermal, Pulsed High Peak Power, High Frequency, Electromagnetic Energy Therapy	124
Flynn DM #97/050	O	Unintended Pregnancy Prevention Program	125
Harris MD #96/079	C	Operational Medical Database Investigation	126
Hauger FH #97/048	O	The Impact of Flowsheets on the Delivery of Preventive Care	127
Marshall RC #95/149	O	Primary Prevention of Otitis Media Using a Parental Education Model to Reduce Risk Factors	128
Martin DC #95/177	C	Comparison of Manipulative Treatment and Conservative Measures in the Management of Carpal Tunnel Syndrome (CTS)	129

PI and No.	Status	Title	Page
Miser WF #96/130	C	Determining the Need for Teaching Interns About Professional Boundaries in the Physician-Patient Relationship	130
Morgan ED #97/101	O	Postresidency Army Family Practice Inpatient Care and Implications on Residency Training	131
Terrio HP #96/053	C	The Annual Pap Smear Screen: Knowledge by Women Soldiers	132
Woolman BA #96/090	O	Treatment of Nocturnal Leg Muscle Cramps: A Double-Blind Placebo-Controlled Crossover Trial of Magnesium Oxide	133
Yetter JF #96/150	C	Characteristics of Outstanding Teachers of Primary Care Medicine in the U.S. Military	134
<b>Department of Medicine, Cardiology Service</b>			<b>135</b>
Arendt MA #96/069	O	Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)	136
Arendt MA #95/068	C	A Double-Blind, Placebo Controlled, Randomized, Dose Response Study of Oral dl-Sotalol Hydrochloride for the Maintenance of Sinus Rhythm in Subjects with Prior Symptomatic Atrial Fibrillation or ....	137
Arendt MA #97/142	O	A Parallel Dose-Response Study of Sustained-Released Moxonidine in Patients with Congestive Heart Failure	138
Arendt MA #97/024	C	A Randomized, Open-Label, Active-Controlled, Multicenter Phase III Safety Study of Two Doses of NATRECOR hBNP Administered As A Continuous Infusion in the Treatment of Decompensated CHF	139
Hicks KA #97/007	O	Antiplatelet Therapy vs Lovenox plus Antiplatelet Therapy for Patients with an Increased Risk of Stent Thrombosis (ATLAST)	140
Mascette AM #97/140	O	A Double-Blind, Placebo-Controlled, Parallel Design Study to Determine the Effect of 75 or 100 mg of Orally Administered Azimilide Dihydrochloride versus Placebo on Survival in Recent Post-MI....	141
Mascette AM #96/141	C	A Phase II, Randomized, Open-Label, Multicenter, International, Angiographic Trial of the Efficacy of TNK-tPA Compared with Accelerated Activase Alterplase rt-PA in Acute Myocardial Infarction.....	142
McHenry JA #96/149	C	ST Segment Depression in Localizing Regional Myocardial Ischemia in Unstable Angina	143
Miller SE #96/073	O	Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Intracoronary Administration of High Osmolar Contrast Agents	144
Olson JP #96/037	O	Impact of Aorto-Coronary Bypass Graft Markers on Graft Patency: A Prospective Trial	145

PI and No.	Status	Title	Page
Stajduhar KC #95/169	C	A Multicenter, Randomized, Parallel, Double-Blind Study to Investigate the Safety and Clinical Efficacy of MK-383 Alone and MK-383 in Combination with Heparin vs. Heparin Alone in Patients with ....	146
Stajduhar KC #96/082	T	Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Transcatheter Coronary Revascularization Procedures	147
Wicks AB #97/032	C	Why Don't Cardiothoracic Surgeons Routinely Use Aorto-Coronary Graft Markers? A Survey of the Members of the Society of Thoracic Surgeons	148
<b>Department of Medicine, Endocrinology Service</b>			<b>149</b>
LeMar HJ #96/083	O	The Polar T3 Syndrome: Metabolic and Cognitive Manifestations, Their Hormonal Regulation and Impact Upon Performance	150
LeMar HJ #96/146	C	Triiodothyronine Serum Kinetics: A New Nonisotopic Method for Field and Clinical Use	151
LeMar HJ #97/124	O	The Effect of Partial Energy Restriction on the Changes in Metabolic and Kinetic Measures of Thyroid Hormone Metabolism During Antarctic Residence	152
<b>Department of Medicine, Gastroenterology Service</b>			<b>153</b>
Carrougher JG #96/026	T	A Double-Blind Trial of Omeprazole versus Placebo for Prophylaxis of Sclerotherapy-Associated Esophageal Ulcer	154
Fincher RK #94/086	T	The Location of the Esophageal Lesion Responsible for Dysphagia. How Accurate is the Patient's History?	155
Tsuchida AM #96/164	O	Epidemiology of Gallbladder Sludge and Stones in Pregnancy	156
Tsuchida AM #96/093	C	A Multicenter Randomized, Double-Blind, Evaluation of Helicobacter pylori Eradication Following Oral GR122311X in Combination with Clarithromycin Compared to Omepraole in Combination with Clarith.....	157
Tsuchida AM #97/012	O	A Pre-Clinical Research and Development Study to Evaluate Stool Specimens for Basement Membrane Fragments/Complexes and Cytoskeletal Proteins	158
<b>Department of Medicine, Hematology/Oncology Service</b>			<b>159</b>
Bertram KA #94/055	C	Agreltin (Anagrelide) for Patients With Thrombocythemia	160
Bertram KA #96/049	O	An Open-Label, Long-Term, Multicenter Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough or Incident Pain in Cancer Patients Previously Enrolled in Other OTFC Studies	161

PI and No.	Status	Title	Page
Bertram KA #97/025	O	Efficacy and Tolerability of 2.5 mg Itasetron Orally and of 32 mg Ondansetron Intravenously in the Prevention of Vomiting and Nausea in Patients Undergoing Cisplatin (> 75 mg/m <sup>2</sup> ) Containing.....	162
Bertram KA #97/111	O	A Multicenter, Double-Blind, Crossover Study of Oral Transmucosal Fentanyl Citrate (OTFC) Compared to Immediate Release Morphine Sulfate for the Treatment of Breakthrough Pain in Cancer Patients ....	163
Bertram KA #97/123	O	Efficacy and Tolerability of 2.5 mg Itasetron IV and 32 mg Ondansetron Intravenously in the Prevention of Vomiting and Nausea in Patients Undergoing Cisplatin Containing Chemotherapy. A Randomized....	164
Bertram KA #97/112	O	An Open-Label, Long-Term, Multicenter Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough or Incident Pain in Cancer Patients Previously Enrolled in AC 600 Series...	165
Bertram KA #94/017	O	Evaluation of Immunity to Breast Cancer	166
Bertram KA #95/099	C	Phase III Trial of 3-Hour versus 96-Hour Infusions of Paclitaxel from NaPro/Baker Norton in Patients with Refractory Metastatic Breast Cancer, and an Assessment of 96-Hour Infusions in 3-Hour Failures	167
Caton JR #95/187	C	A Study to Evaluate the Effect of Cisplatin/Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment of Goals in Accessible Tumors of Any Histology	168
Hu JSD #95/133	C	A Double-Blind, Randomized, Phase 3, Multicenter Study of Suramin and Hydrocortisone vs Hydrocortisone and Placebo in the Treatment of Patients with Metastatic, Hormone-Refractory Prostate Carcinoma	169
Jones MP #97/138	O	Phase 2/3 Placebo Controlled Trial of Targretin Capsules (LGD1069) in Patients with Advanced Non-Small Cell Lung Cancer	170
Williams RF #95/170	C	Phase 3 Trial of Gemcitabine Plus Cisplatin Versus Cisplatin Alone in Patients with Metastatic Non-Small Cell Lung Cancer	171
Williams RF #95/138	O	The Effect of Tamoxifen and Ionizing Radiation on Expression of Bcl-2, Bcl-x, and p53 in Breast Cancer Cells In Vitro	172
Williams RF #95/162	O	The Characterization of Breast Cancer Susceptibility Genes in Males and Their Kindred	173
Williams RF #94/118	C	Phase II Study of Single Agent Thiotepa for Advanced, Hormone-Refractory Prostate Carcinoma	174

PI and No.	Status	Title	Page
Williams RF #97/026	O	A Phase II Trial of Thioplex Following Induction Chemotherapy to Decrease the Incidence of Brain Metastases in Limited Stage Small Cell Lung Cancer Patients	175
Williams RF #97/040	T	Multicenter, Open-Label, Randomized, 2-Arm, Phase II Trial of Letrozole (2.5 mg p.o. q.d.) versus the Combination of Letrozole (2.5 mg p.o. q.d.) + Tamoxifen (20.0 mg p.o. q.d.) As First-Line ....	176
Williams RF #97/110	O	Double Blind, Double Dummy, Randomized, Multicenter, 2-Arm, Phase III Trial Comparing Letrozole 2.5 mg versus Tamoxifen 20 mg as First Line Therapy in Postmenopausal Women with Advanced Breast Cancer	177
<b>Department of Medicine, Infectious Disease Service</b>			<b>178</b>
Cooper RH #95/132	C	An Open-Label, Multicenter Study of Clinafloxacin in the Treatment of Infective Endocarditis	179
<b>Department of Medicine, Internal Medicine Service</b>			<b>180</b>
Fincher RK #97/008	T	Are Sputum Cultures Useful in the Management of Uncomplicated Community-acquired Pneumonia	181
Fincher RK #97/049	C	Are Hemoglobins and Potassiums Drawn From Intravenous Heparin Locks Accurate?	182
Fincher RK #97/113	O	Optimal Bowel Preparation for Flexible Sigmoidoscopy: Oral Magnesium Citrate with Oral Bisacodyl or with Two Hypertonic Phosphate Enemas	183
Gibbons RV #97/016	O	A Controlled Clinical Trial to Improve Housestaff Identification of and Attitudes Toward Mental Disorders in Primary Care	184
Jackson JL #96/156	C	A Pilot Study of the Semmes-Weinstein Monofilament for Diagnosing Peripheral Neuropathy in Diabetics: Inter-rater Reproducibility and Comparison with Standard Clinical Examination	185
Jackson JL #96/161	C	The Relationship Between Intensity of Anticoagulation and Complications	186
Jackson JL #96/155	C	Symptom Related Expectations in A Rheumatology Clinic Setting	187
Leclerc KM #95/048	T	The Effect of Left Ventricular Hypertrophy on Diastolic Function at Rest and After Exercise	188
Lesho EP #96/091	T	Can Antibody Response to Pneumococcal Vaccination Be Enhanced by Pretreatment with Vitamin B12	189
Osgard EM #96/070	C	Optimal Bowel Preparation for Flexible Sigmoidoscopy: Hypertonic Phosphate Enemas with and Without Use of Oral Magnesium Citrate or Tap Water Enemas	190

PI and No.	Status	Title	Page
Stuart EB #96/109	O	Coronary Artery Calcification Detected with Computed Radiography as a Marker for Obstructive Coronary Artery Disease	191
<b>Department of Medicine, Neurology Service</b>			<b>192</b>
Beaver GW #96/007	T	Ophthalmic Anesthesia in Trigeminal Neuralgia	193
Bolt JL #97/137	O	Clinical Experience and Use of Vigabatrin (Sabril) in Patients with Infantile Spasms	194
Bolt JL #97/083	O	Compassionate Use of Vigabatrin in Infantile Spasms	195
Newmark J #94/129	T	The Assessment of Motor Recovery After Stroke Induced Hemiplegia	196
<b>Department of Medicine, Pulmonary Service</b>			<b>197</b>
Caras WE #97/057	O	The Use of Ipratropium Bromide (Atrovent) in COPD Exacerbation	198
Collins DM #90/099	O	Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure	199
Dillard TA #97/076	C	A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Pulmicort (Budesonide) Turbuhaler, 400 mcg Administered Once Daily for 12 Weeks, in Adult Patients with Inhaled Steroid....	200
Giacoppe GN #97/087	O	A Phase 2 Study to Determine the Safety, Pharmacokinetics, and Effective Dose Range and Dosing Duration for Recombinant Activated Protein C (rAPC) in Severe Sepsis	201
Grathwohl KWA #96/138	S	Active Inspiration/Expiration versus Tidal Volume Breathing During Transbronchial Biopsy	202
Grathwohl KWA #94/029	O	A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation	203
Regan NA #96/004	T	Controlled Prospective Evaluation of Intrapulmonary Percussive Ventilation with Standard Chest Physiotherapy	204
Roth BJ #91/015	O	Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure	205
Roth BJ #97/132	O	Respiratory Care Team to Decrease the Misuse of Metered Dose Inhalers in Hospitalized Patients	206
Roth BJ #95/172	C	The Value of Questionnaire Responses and Body Measurements in the Prediction of Obstructive Sleep Apnea in a Young Physically Fit Population	207

PI and No.	Status	Title	Page
Roth BJ #92/024	O	Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging	208
<b>Department of Nursing</b>			<b>209</b>
Bianchi AM #97/067	T	Increased TMC Access to Urinary Incontinence Therapy	210
Chapman JB #97/003	C	Effect of Prophylactic Preoperative Intravenous Caffeine Administration on the Incidence of Postoperative Headache in the Daily Caffeine User	211
Feider LL #97/131	O	Risk Factors for Nosocomial Pneumonia	212
Forsythe MA #97/078	C	Expert Power and Decision Making in Nurse Managers: A Test of the Theory of Planned Behavior	213
Heiner SL #97/068	O	Effects of Stress Responses on Wound Healing	214
Heiner SL #94/100	C	Postoperative Wound Healing: Hydration and Oxygenation	215
Heiner SL #96/112	O	Wound Healing: The Effect of Supplemental Oxygen Therapy	216
Hildreth PJ #97/077	O	Linking Nursing Care to ANA Quality Indicators	217
Hildreth PJ #96/132	O	Pressure Ulcer Prevention: Comparing Support Surfaces	218
Jennings BLM #96/122	T	A Grounded Theory Analysis of Patient Satisfaction in the Military	219
Jennings BLM #96/125	O	A Survey of Access to Care in the TRICARE Environment	220
Jennings BLM #97/063	T	Caregiver Interactions and Patient Satisfaction	221
Loan LA #93/117	C	Exogenous Surfactant Therapy in Premature Infants	222
Loan LA #95/175	C	A Comparison of Skin Microbes Under Two Types of Temperature Probe Covers Used on Premature Newborns	223
Loan LA #95/190	O	The Effects of Thermocouple Sensor Placement on Neonatal Skin Temperature Measurement	224
Loan LA #96/137	O	Single Woman's Breast Cancer Program	225
McCarthy MS #95/076	O	Gastric/Jejunal Feeding: Nutritional Outcomes and Pneumonia	226
Miller TH #96/128	T	Natural Killer Cell Activation in Women with Early Stage Breast Cancer	227

PI and No.	Status	Title	Page
Mittelstaedt EA #97/066	S	Postpartum Physical Fitness in Military Women	228
Moore CJ #97/082	C	Deployment Competency and Skill Retention of Anesthesia Care Providers Using the Field Anesthesia Machine	229
Moureau PM #97/015	C	Social Support of Women Treated for Breast Cancer	230
Moureau PM #97/106	O	Natural Killer Cell Activation and Apoptosis in Women with Early Stage Breast Cancer: Potential Measure for Nursing Research	231
Renaud MT #93/115	C	Neonatal Outcomes in a Modified NICU Environment	232
Renaud MT #94/101	C	Fatigue Following Childbirth: Military Family Outcomes	233
Riley ME #96/148	C	Feasibility and Patient Satisfaction with Wearing an Eye Mask and Ear Plugs During Regular Sleep Times While in the Coronary Care Unit	234
Schempp CM #95/079	C	Soldier HIV Behavior Modification	235
Spence LL #97/079	C	Determination of Key Events in Female Military Adolescents' Lives Which May Predispose Them to Depressive Episodes	236
Wilson SK #97/010	C	Impact of a Research Project on Clinical Practice: Year Three Evaluation	237
<b>Department of Obstetrics/Gynecology</b>			<b>238</b>
Calhoun BC #96/136	C	Teen Pregnancy	239
Davis GD #97/108	O	Transanal Ultrasonography (TAUS) in the Repair of Episiotomy Anal Sphincteroplasty	240
Davis GD #97/107	O	The Effectiveness of Mechanical Devices in the Prevention of Exercise Induced Urinary Incontinence in the Female Soldier	241
Davis GD #95/129	O	The Non-invasive Detection and Characterization of Anal Incontinence in the Parous Female Population	242
Davis GD #96/038	C	Ambulatory Recording of Urodynamic Functioning in Female Soldiers During Training	243
Davis GD #96/084	T	Incidence of Exercise Related Musculoskeletal Injuries vs Phase of the Menstrual Cycle	244
Hoeldtke NJ #97/035	C	The Effects of Adrenomedullin and Angiotensin II on Fetoplacental Vascular Tone	245
Hoeldtke NJ #97/080	C	The Vasoactive Effects of Adrenomedullin on Fetoplacental Vasculature Precontracted with Endothelin-1 or the Thromboxane Mimetic, U46619	246



PI and No.	Status	Title	Page
Hume RF #92/101	C	Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy	247
Potter ME #97/144	O	Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig ( <i>Sus scrofa</i> )	248
Potter ME #94/085	T	Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig ( <i>Sus scrofa</i> ) and Goat ( <i>Capri hircus</i> )	249
Rondeau JA #96/051	T	Caesarean Section Pain Study	250
Shrout AB #94/138	T	Once vs Thrice Daily Gentamicin Dosing in Postpartum Endomyometritis	251
Wagner RK #97/114	O	The Effects of Lipopolysaccharide, an Inflammatory Stimulus, on Placental Production of Interleukin 6 in the Isolated Dually Perfused Placental Cotyledon	252
Wagner RK #97/044	C	Plasma Levels of Adrenomedullin, A Hypotensive Peptide, in the Fetoplacental Circulation	253
<b>Department of Pediatrics</b>			<b>254</b>
Baechler VR #95/085	O	Parental Assessment of Psychologic Adjustment in Children with Asthma: A Comparison of the Child Behavior Checklist and the Behavior Assessment System for Children	255
Carter ER #95/137	C	The Relationship of Positive Skin Tests to House Dust Mite, Grass Pollen, and Cat Dander to Asthma in Children Presenting to a Pediatric Pulmonary Clinic	256
Carter ER #97/126	O	Long-Term Use of Every 4-8 Week Intramuscularly Administered Triamcinolone Acetonide to Treat a 13 Year-Old Who Has Severe, Life-Threatening Chronic Asthma	257
Fairchok MP #90/092	O	Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses	258
Gries DM #96/060	C	Single Dose Intramuscular Dexamethasone Acetate vs. Oral Prednisone to Treat Exacerbations of Asthma in Young Children	259
Hinson RM #97/004	C	Evaluation of Anti-inflammatory Actions of Perfluorophenanthane	260
Hinson RM #96/080	C	MgSO <sub>4</sub> Therapy for the Prevention of Intracranial Hemorrhage and Cerebral Palsy in the Very Low Birthweight Infant: Role of Interleukin-6	261
Hinson RM #94/025	T	Fetal Development: Are Undiagnosed Maternal Inborn Errors of Metabolism Associated With Poor Intrauterine Growth and Congenital Malformations in the Developing Fetus	262

PI and No.	Status	Title	Page
Sweeney JK #97/056	O	Physiological, Behavioral, and Feeding Effects of Neonatal Physical Therapy Procedures on Preterm Infants in a Neonatal Intensive Care Unit Setting	263
Trementozzi DP #96/008	C	Effect of Short Course High Dose Corticosteroids on the Immune Response to the Influenza Vaccine in a Pediatric Population	264
<b>Physical Medicine and Rehabilitation Service</b>			<b>265</b>
Burke LC #96/098	C	A Randomized Clinical Trial of A Home Program Monitored by a Physical Therapist versus Repeated Outpatient Physical Therapy Visits Combined with Home Program to Treat Stiff Shoulder	266
Kumar SJ #96/152	O	Cervical and Lumbar Radiculopathies: How Many Muscles Should Be Studied?	267
Lauder TD #96/023	T	Deep Water Running as A Form of Rehabilitation for Ankle Inversuib Sprains: A Look at Maintenance of Land Based Running Performance and Long Term Training Effects	268
Lauder TD #96/006	C	The Female Athlete Triad: Prevalence in Military Women	269
Dettori JR #94/157	C	The Effect of Pregnancy on the Performance, Health, and Nutritional Status of Postpartum Soldiers	270
Norvell DC #97/037	C	The Effects of Transcutaneous Electrical Nerve Stimulation on Delayed Onset Muscle Soreness	271
<b>Preventive Medicine Service</b>			<b>272</b>
Gunzenhauser JD #95/011	O	Comparative Morbidity Study of Active Duty Women Serving in Korea and Ft Lewis by MAJ Jeffrey D. Gunzenhauser, MC	273
Niebuhr DW #97/019	C	The Risk of Myocardial Infarction Associated with Physical Inactivity in Young Women	274
Rumm PD #96/159	C	Relationship of Spouse and Child Abuse in A Military Population	275
<b>Department of Psychology</b>			<b>276</b>
Lambie MG #97/001	C	Neurocognitive Functioning in Children with Chronic Idiopathic Thrombocytopenic Purpura	277
Lester KS #95/130	O	MMPI-2 Profiles in Korean Military Dependents	278
Masson JR #96/103	C	Reports, Estimates, and Tests Results of Memory Functioning in Children With and Without ADHD: Concordance Between Self-Report, Parent-Report, Teacher-Report, and Test Results	279
Powell JB #94/108	T	Medical Cost Offset and Clinical Effectiveness of a Behavioral Treatment Program for Medical Resource Overutilizers	280

PI and No.	Status	Title	Page
<b>Department of Radiology</b>			<b>281</b>
Bauman JM #93/119	O	Gallbladder Ejection Fractions	282
Bauman JM #94/077	T	Determination of Normal Regional Myocardial Thallium Distribution and Development of a New Display Technique	283
Bender GN #94/038	O	Digitally Acquired Radiographic Air Contrast Barium Enema vs. Colonoscopy in Polyp Detection, Cancer Detection, and cost in a Federal Tertiary Care Center	284
Casha LM #97/034	C	Benign and Malignant Soft Tissue Tumors. Do Certain Tumors Tend to Occur in Certain Locations and Are Certain Tumors More Common in Certain Ages?	285
Varma MK #96/081	O	Pulmonary Manifestations of Gastro-esophageal Reflux Disease: HRCT Findings	286
Makuch RS #95/166	O	Cost Effectiveness of Early MRI in Traumatic Wrist Injury	287
Mansfield LT #97/046	C	Intravenous Contrast-Enhanced MR Saline Arthrography: A Technique for Staging Juxta-articular Masses	288
Morgan RE #97/027	O	Helical Computed Tomography Oral Cholecystography (HCT-OCG) vs. Ultrasound (US) in the Detection of Cholelithiasis	289
Shaves ME #96/076	O	Effectiveness of Oral Dolasetron Mesylate (50 mg) versus Prochlorperazine in the Treatment of Nausea and Emesis Due to Fractionated Abdominal Radiotherapy	290
Timmons JH #97/043	T	Comparison of CO <sub>2</sub> , Water Soluble Contrast, and Water Soluble Contrast with Methyl-Cellulose During Computed Tomographic Enteroclysis Using a Porcine Model	291
Varma MK #96/142	O	Radiologic Guided Aspiration of Intra-articular Ganglia in the Knee	292
Walsh DW #97/045	C	Comparison of CT-Enteroclysis and Traditional CT in the Setting of Suspected Partial Small Bowel Obstruction	293
Whitaker MA #97/023	T	Validation of Nipple Arc Lesion Localization Technique	294
<b>Department of Surgery, Cardiothoracic Surgery Service</b>			<b>295</b>
Heric BR #94/156	T	North American Duraflow II Working Group	296
<b>Department of Surgery, General Surgery Service</b>			<b>297</b>
Brown TA #95/108	C	Telomerase Activity and Expression of p53, DCC, and Rb in Human Colorectal Cancer	298

PI and No.	Status	Title	Page
Brown TA #95/106	T	Telomerase Activity and Telomere Length in Human Breast Cancer	299
Brown TA #97/064	O	Prognostic Significance of p53 Mutations in the Lymph Nodes of Dukes B Colon Cancer Patients	300
Brown TA #97/141	O	A Prospective Multi-institutional Study to Determine the Sensitivity and Specificity of Telomerase in ERCP Brushings for Detection of Pancreatic and Biliary Cancer	301
Brown TA #97/143	O	A Prospective Multi-institutional Study to Determine the Sensitivity and Specificity of Telomerase in Thyroid FNAs for the Detection of Thyroid Cancer	302
Brown TA #96/009	O	Postoperative Cisapride Therapy After Colorectal Surgery	303
Carter PL #97/047	O	Genetic Testing for Inherited Cancer	304
Chung MH #95/119	C	C-Reactive Protein in the Diagnosis of Acute Appendicitis	305
Chung MH #96/045	S	The Effect of Low-Dose Dopamine on Splanchnic Blood Flow with Intra-abdominal Hypertension in Domestic Yorkshire Swine, <i>Sus scrofa</i>	306
Eggebroten WE #95/038	O	Advanced Trauma Life Support Course Utilizing the Goat ( <i>Capra hircus</i> )	307
Eggebroten WE #95/035	O	Madigan Army Medical Center Institute for Advanced Endoscopic Training Using the Pig ( <i>Sus scrofa</i> )	308
Hansen BR #95/022	O	The Use of Autologous Fibrin Glue to Prevent Post-operative Seromas in Patients Undergoing modified Radical Mastectomy	309
McDonald JM #96/099	T	Evaluation of Multiple Metastatic Tumor Sources for Mutation of Human Metastasis Suppressor Gene KAI1	310
Peterson AC #97/148	C	Outcomes of Varicocele Ligation Done For Pain: A Chart Review	311
Rooney RC #95/142	T	Development of An Animal Model for a Simple Bone Cyst in the Goat	312
Rooney RC #95/141	S	Development of a Pig Model to Produce a Growing Fused Limb by Transferring Half of the Open Growth Plate From the Lower End of the Femur to the Upper End of the Tibia When the Tibia's Growth Plate....	313
Watts DM #95/184	T	A Phase II Study to Evaluate LY320052 (rHb1.1) Compared to Standard Allogeneic Blood Transfusion Therapy in Elective Surgery	314
Williard WC #97/135	O	Linezolid (PNU-100766) in the Treatment of Gram Positive Bacteremia: An Open Label Phase II Study of Intravenous Therapy with Optional Oral Continuation	315

PI and No.	Status	Title	Page
Williard WC #97/122	O	Linezolid in the Treatment of Skin/Soft Tissue Infections: An Open Label, Randomized, Dose Comparative Phase II Study of Low Dose Linezolid	316
Williard WC #96/032	C	Phase III Population Pharmacokinetic Study for the Determination of Plasma Levels of Synercid (quinupristin/dalfopristin) in Treated Patients (Protocol JRV-135)	317
<b>Department of Surgery, Ophthalmology Service</b>			<b>318</b>
Chismire KJ #97/086	O	A 6-Month, Randomized, Double-Masked Comparison of Fixed Combination of Latanoprost and Timolol with the Individual Components, Continuing into a 6-Month Open Label Safety Study of Fixed Combination...	319
Chismire KJ #97/065	O	A Parallel, Randomized, Double-Masked, Active Controlled, Multiclinic Study Comparing the Tolerability and Efficacy of 2.0% Dorzolamide Ophthalmic Solution and Orally Administered Acetazolamide in....	320
Chun BB #97/060	O	Radial Keratotomy and Phototherapeutic Keratectomy: Comparison of Corneoscleral Integrity After Controlled Blunt Trauma to Post Mortem Eyes That Had Refractive Surgery	321
Chun BB #97/011	C	Bovine Pericardium and Fascia Lata: Comparison in Physical Characteristics	322
George RK #96/140	C	A Parallel, Randomized, Double-Masked, Multicenter Study Comparing the Effect of Dorzolamide 2% to Pilocarpine 2% as Adjunctive Therapy to Timolol Maleate Ophthalmic Gel Forming Solution 0.5% in ....	323
Mader TH #96/061	T	The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia	324
Mader TH #97/119	O	The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia	325
Mader TH #96/153	O	Refractive Changes at High Altitude More Than Four Years Following Radial Keratotomy	326
Mazzoli RA #94/125	C	Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by Magnetic Resonance (MR) and Computed Tomography (CT) Imaging in the Goat	327
Nelson ML #97/121	O	Refractive Changes During Exposure to the Hyperbaric Environment Following Radial Keratotomy Surgery	328
Nelson ML #97/105	C	Ocular Findings in Robinow (Fetal Face) Syndrome	329
Torres MF #96/029	T	A Prospective, Randomized Clinical Trial Comparing Topical Prednisolone 1% to Diclofenac 0.1% in the Treatment of Pseudophakic Cystoid Macular Edema (PCME)	330
Torres MF #97/081	C	The Contribution of the Donor Cornea to Final Corneal Curvature in Penetrating Keratoplasty	331

PI and No.	Status	Title	Page
Torres MF #97/017	C	Pseudotumor Cerebri Associated with Minocycline Therapy	332
Wroblewski KJ #96/135	C	Anterior Capsular Contraction in Phacoemulsification	333
Wroblewski KJ #96/154	C	Pulfrich's Phenomenon in Patients with Optic Neuropathy	334
<b>Department of Surgery, Orthopedics Service</b>			<b>335</b>
Bal GK #97/052	C	Does Insertion of a Cortical Bone Screw Into Bone Change the Torsional Strength? A Biomechanical Study	336
Bal GK #97/051	O	Comparison of Small Bone Cannulated Screw Systems	337
Bal GK #97/094	O	Autologous Cartilage Grafting for Talar Dome OCT Lesions	338
Bal GK #96/107	O	Evaluation of Lateral Ankle Stress Testing With and Without Anesthesia	339
Bal GK #96/108	O	Subtalar Joint Stress Radiography	340
Bal GK #97/095	O	Delayed versus Immediate Open Repair of Achilles Tendon Rupture	341
Cannon CP #97/098	O	Fixation of Salter Osteotomies with Bioabsorbable Pins	342
Carpenter CT #95/110	C	A Multicenter Study of Treatment of Growth Arrest by Excision of Physeal Bars	343
Carpenter CT #94/176	O	Computer Assisted Measurement of Scoliosis from Digitized Radiographs versus Traditional Cobb Angle Measurement	344
Hildebrand RK #95/082	S	Comparison of Sterile Isotonic Saline, Purified Water, and Dilute Hypochlorite Solution on the Rates of Infection and Tissue Response in Open Fractures of a Syrian Hamster Model	345
Hildebrand RK #94/142	T	Cost Effectiveness of Screening MRIs of the Shoulder Prior to Neer Acromioplasties	346
Johnstone FL #95/102	O	Teaching Program for Practical Microsurgery Using A Rat ( <i>Rattus norvegicus</i> , strain HSD) As a Teaching Model	347
Jones DEC #95/128	T	Use of Pulsing Electromagnetic Fields to Potentiate Healing of Traumatic Combat and Training Injuries	348
Jones DEC #95/155	O	Establishment of the Natural History/Progression of Pediatric Fingernail Injury Outcomes	349
Noonburg GE #97/125	O	External Fixation of Displaced Clavicle Fractures	350
Pitcher JD #96/111	C	Economic Evaluation of Scotchcast Plus vs Plaster of Paris for Immobilization of Fracture of the Arm and Leg	351

PI and No.	Status	Title	Page
StPierre P #96/092	O	A Prospectively Randomized Study on the Effectiveness of Post-Operative Knee Bracing for Anterior Cruciate Ligament Reconstruction	352
StPierre P #96/086	O	A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough	353
Willard K #95/174	T	Comparative Effectiveness of (a) Standard Treatment, (b) Standard Treatment Plus Force Measured Orthotic Cutting Methodologies, (c) Standard Treatment Plus Pulsing Electromagnetic Fields, and (d) A ..	354
Williamson RV #97/099	O	Tendon-Healing to Cortical Bone After Tendon Reattachment Using Suture Anchors. A Biomechanical and Histological Evaluation in Goats	355
<b>Department of Surgery, Otolaryngology Service</b>			<b>356</b>
Edmond CV #96/157	O	Clinical Investigation of Viewpoint in Image-Assisted Surgery	357
Edmond CV #94/177	O	ENT Surgical Simulator Project	358
Kanne TJ #96/134	C	Universal Screening of Hearing Loss Using Transient Evoked Otoacoustic Emissions	359
Mesaros GJ #95/040	C	The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas	360
Perkins JA #96/075	T	Recurrent Acute Otitis Media: Treatment and Outcomes	361
Perkins JA #96/044	O	Pediatric Brochoesophagology Laboratory Using Swine (Sus scrofa)	362
Ruegemer JL #97/002	C	Experimental Model of the Palmaz Expandable Metallic Stent in the Trachea of Pigs (Sus scrofa)	363
Thomas RW #97/085	O	Immediate Extubation/Decannulation Following Laryngotracheoplasty Using Metallic Expandable Stents in the Pig (Sus scrofa) Airway	364
Thomas RW #97/084	O	Inflammatory Response Related to Tracheobronchial Distention in Pigs (Sus scrofa) Using Expandable Metallic Stents	365
Ulnick KM #97/115	C	Perioperative Management of the Obstructive Sleep Apnea Patient	366
<b>Department of Surgery, Urology Service</b>			<b>367</b>
Ellsworth JB #97/036	O	Experience with the Dornier U50 Lithotripter	368
Feber KM #97/014	C	A Retrospective Review of Vasovasostomy Using Loupe Magnification	369
Lance RS #95/104	O	Telomere Length and Telomerase Activity in Human Testicular Cancer	370

PI and No.	Status	Title	Page
Lance RS #97/097	O	Telomerase Activity in Voided Urine and Bladder Washings As A Diagnostic and Surveillance Marker for Transitional Cell Carcinoma	371
Lance RS #95/109	C	Telomere Activity and Expression of p53 and Rb in Human Transitional Cell Carcinoma	372
Lance RS #97/069	O	Vibratory Stimulated Bladder Cell Exfoliation in Voided Urine	373
O'Reilly KJ #97/129	O	The Correlation Between Free and Total PSA, Prostate Specific Membrane Antigen and Sex Hormone Binding Globulin Across the Spectrum of Prostate Disease	374
O'Reilly KJ #97/038	C	Concomitant Use of the Erection Vacuum Device and Penile Prosthesis	375
O'Reilly KJ #96/129	O	Oral Ciprofloxacin for Acute Prostatitis	376
Ruiz HE #97/136	O	The Protegen Sling for the Treatment of Female Stress Urinary Incontinence: A Pilot Study	377
Ruiz HE #96/158	O	Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis	378
Soderdahl DW #96/100	C	Comparison of Five Second Urinary Home Flow Rates to Formal In-Office Uroflowmetry	379
Thrasher JB #96/113	O	Relief Strategies for Initiative Bladder Symptoms Associated with Intravesical BCG - A Pilot Study	380
Thrasher JB #96/002	C	Measurement of Irritative Bladder Symptoms	381
Thrasher JB #97/130	O	Immunity in Prostate Diseases	382
Thrasher JB #94/164	O	Prostate Cancer Intervention vs Observation Trial (PIVOT): A Randomized Trial Comparing Radical Prostatectomy vs Palliative Expectant Management for the Treatment of Clinically Localized Prostate ...	383
Thrasher JB #95/134	O	Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin: 250 mg Q8h vs 500 mg QD	384
Thrasher JB #95/083	T	Diet and Prostate Hormones	385
Thrasher JB #97/147	O	Comparison of Quality of Life (QOL) Differences Between Radical Retropubic (RRP) and Radical Perineal Prostatectomy (RPP) for Clinically Localized Prostate Cancer	386
Thrasher JB #95/150	C	Center for Prostate Disease Research Prostate Cancer Radical Prostatectomy Follow-up Questionnaire	387
Thrasher JB #97/120	O	A Randomized, Double-Blind Study (With Open-Label Treatment Extension) to Evaluate the Efficacy and Safety of VIAGRA (Sildenafil) in Erectile Dysfunction	388



PI and No.	Status	Title	Page
Thrasher JB #94/051	O	Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer	389
Thrasher JB #97/039	O	A Multicenter, Phase II, Placebo-Controlled Pilot Study of SNX-111 Administered Intrathecally to Patients with Acute Postoperative Pain	390
Thrasher JB #94/144	C	Evaluation of the Safety and Efficacy of Transurethral Resection of the Prostate Using the Contact Laser System vs Electrosurgery	391
<b>Department of Surgery, Vascular Surgery Service</b>			<b>392</b>
Andersen CA #96/163	O	Clinical Evaluation of the Handling and Performance of the HEMASHIELD Knitted Double Velour Fabric and Polytetrafluoroethylene (PTFE) Patched for Carotid Endarterectomy Patch Procedures in Patients	393
Tollefson DFJ #95/097	O	Abdominal Aortic Aneurysm (AAA) and Chronic Obstructive Pulmonary Disease (COPD)	394
<b>Social Work Service</b>			<b>395</b>
Mitchell GT #97/100	O	Comparison and Prediction of Completers and Non-completers of A Domestic Violence Program	396
Raiha NK #97/061	C	An Assessment of the Characteristics of Spouse Abuse in A Military Population	397
Raiha NK #96/139	C	Spouse Abuse Among Active Duty Women Married to Civilian Husbands: An Examination of Interpersonal and Social Factors	398
<b>Gynecology Oncology Group</b>			<b>399</b>
Potter ME #82/073	O	GOG 0026A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies	400
Potter ME #82/007	O	GOG 0026C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies	401
Potter ME #91/008	O	GOG 0026II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies	402
Potter ME #93/153	O	GOG 0026LL: A Phase II Trial of Prolonged Oral Etoposide (VP-16) in Patients With Advanced Pelvic Malignancies	403
Potter ME #81/035	O	GOG 0041: Surgical Staging of Ovarian Carcinoma	404
Potter ME #81/105	O	GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma	405

PI and No.	Status	Title	Page
Potter ME #84/033	O	GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease	406
Potter ME #84/074	O	GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the ...	407
Potter ME #86/089	O	GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and...	408
Potter ME #87/013	O	GOG 0090: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors	409
Potter ME #87/104	O	GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy	410
Potter ME #89/036	C	GOG 0093: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)	411
Potter ME #87/028	O	GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III	412
Potter ME #87/091	O	GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma	413
Potter ME #89/052	O	GOG 0108: Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #113891) with or without Cisplatin (NSC #119875) in Patients with Advanced or Recurrent Mixed Mesodermal Tumors of the Uterus	414
Potter ME #91/086	O	GOG 0109 (SWOG 8797): A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy, versus Radiation Therapy Alone in Selected Patients with Stages ...	415
Potter ME #91/064	T	GOG 0113: An Evaluation of Hydroxyurea, 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative .....	416
Potter ME #91/074	O	GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, ....	417

PI and No.	Status	Title	Page
Potter ME #94/013	C	GOG 0116: Evaluation of Adjuvant VP-16 and Carboplatin Therapy in Totally Resected Ovarian Dysgerminoma	418
Potter ME #93/061	O	GOG 0120: A Randomized Comparison of Hydroxyurea vs Hydroxyurea, 5-FU Infusion and Bolus Cisplatin vs Weekly Cisplatin as Adjunct to Radiation Therapy in Patients with Stages IIB, III, IVA Carcinoma..	419
Potter ME #94/014	O	GOG 0122: Whole Abdominal Radiotherapy Versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma	420
Potter ME #93/063	O	GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix	421
Potter ME #95/064	S	GOG 0126C: A Phase II Evaluation of Altretamine (Hexamethylmelamine) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer	422
Potter ME #96/066	S	GOG 0126D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer	423
Potter ME #96/115	C	GOG 0126E: Evaluation of Paclitaxel and SDZ PSC 833 (IND #41232) in Recurrent, Platinum Resistant and Refractory Ovarian Cancer	424
Potter ME #97/072	O	GOG 0126-G: Evaluation of CI-958 in Recurrent, Platinum Resistant, and Refractory Ovarian Cancer	425
Potter ME #97/073	O	GOG 0126-H: Evaluation of 24-Hour Continuous Infusion Topotecan in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer	426
Potter ME #95/171	O	GOG 0127H: Evaluation of Prolonged Oral Etoposide (VP-16) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix	427
Potter ME #97/091	O	GOG 0127-J: Evaluation of 9-Cis Retinoic Acid (9-CRA, NSC #659772) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix Previously Treated by Chemotherapy	428
Potter ME #94/102	O	GOG 0128B: Evaluation of Paclitaxel (Taxol) in Persistent or Recurrent Non-Squamous Cell Carcinoma of the Cervix and Vagina	429
Potter ME #97/029	O	GOG 0128D: Evaluation of Tamoxifen in Persistent or Recurrent Non-squamous Cell Carcinoma of the Cervix	430
Potter ME #96/068	O	GOG 0129E: Evaluation of Dactinomycin (Cosmegen) in the Treatment of Recurrent or Persistent Endometrial Carcinoma	431
Potter ME #95/027	C	GOG 0130B, Evaluation of Paclitaxel (Taxol) in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus.	432

PI and No.	Status	Title	Page
Potter ME #97/074	O	GOG 0130-C: Evaluation of Trimetrexate in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus	433
Potter ME #94/062	O	GOG 0131B: Evaluation of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus	434
Potter ME #97/075	S	GOG 0131-D: Evaluation of Trimetrexate in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus	435
Potter ME #97/146	O	GOG 0137: A Randomized Double-Blinded Trial of Estrogen Replacement Therapy versus Placebo in Women with Stage I or II Endometrial Adenocarcinoma	436
Potter ME #93/087	O	GOG 0139: A Randomized Study of Doxorubicin Plus Cisplatin versus Circadian-Timed Doxorubicin Plus Cisplatin in Patients with Primary Stages III and IV, Recurrent Endometrial Adenocarcinoma	437
Potter ME #97/092	O	GOG 0141: Treatment of Patients with Suboptimal (Bulky) Stage IB Carcinoma of the Cervix: A Randomized Comparison of Radical Hysterectomy and Pelvic and Para-aortic Lymphadenectomy with or without....	438
Potter ME #93/149	S	GOG 0143: Familial and Reproductive Factors in Ovarian Cancer	439
Potter ME #94/140	S	GOG 0145: A Randomized Study of Surgery vs Surgery + Vulvar Radiation in the Management of Poor Prognosis Primary Vulvar Cancer and of Radiation vs Radiation & Chemotherapy for Positive Inguinal Node	440
Potter ME #95/090	O	GOG 0146C: Evaluation of Topotecan (SKF 104864-A) (NSC#609699) in Recurrent, Platinum, Sensitive Ovarian Cancer	441
Potter ME #96/065	S	GOG 0146D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Sensitive Ovarian Cancer	442
Potter ME #97/102	O	GOG 0146-E: Evaluation of CI-958 in Recurrent, Platinum-Sensitive Ovarian Cancer	443
Potter ME #97/104	O	GOG 0146-F: Evaluation of 24-Hour Continuous Infusion Topotecan in Recurrent and Platinum-Sensitive, or Metastatic Ovarian Cancer	444
Potter ME #94/094	O	GOG 0148: The Clinical Utility of Soluable TNF/LT Membrane Receptors in the Serum of Patients With All Stages of Primary Epithelial Ovarian Cancer	445
Potter ME #94/061	O	GOG 0150: A Phase III Randomized Study of Accelerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) vs Combination Ifosfamide-Mesna With Cisplatin ... Carcinosarcoma (CS) of the Uterus	446

PI and No.	Status	Title	Page
Potter ME #94/150	O	GOG 0152: A Phase III Randomized Study of Cisplatin & Taxol (Paclitaxel) With Interval Secondary Cytoreduction vs Cisplatin and Paclitaxel in Patients with Suboptimal Stage III & V....ovarian carcinom	447
Potter ME #95/028	C	GOG 0154: Human Immunodeficiency Virus (HIV) Testing in Patients with Invasive Cervical Carcinoma.	448
Potter ME #95/029	C	GOG 0155, Evaluation of Alpha-Interferon and Isotretinoin With or Without Zidovudine (AZT) in the Treatment of HIV-Infected Women with Invasive Cervical Carcinoma.	449
Potter ME #95/095	O	GOG 0156: Randomized Trial of Pelvic Radiation versus Doxorubicin Plus Cisplatin in Stage IB, Stage IC, IIA, and IIB EnDometrial Carcinoma	450
Potter ME #95/096	O	GOG 0157: A Randomized Phase III Trial of Carboplatin (AUG 7.5) and Paclitaxel 175 mg/m2 q 21 Days x 3 Courses versus the Same Regimen x 6 Courses in Patients With Selected Stage IC and II (A,B,C)...	451
Potter ME #95/072	O	GOG 0158: A Phase III Randomized Study of A Platinum Compound and Paclitaxel in Optimal Stage III Epithelial Ovarian Carcinoma: Cisplatin vs Carboplatin and 3-Hour vs 96-Hour Infusions of Paclitaxel	452
Potter ME #96/067	C	GOG 0159: A Phase II Study of Goserelin Acetate (Zoladex) in Recurrent or Persistent Endometrial Cancer	453
Potter ME #97/093	O	GOG 0160: Evaluation of Anti-HER2 Antibody in Recurrent or Refractory Ovarian Cancer	454
Potter ME #96/114	O	GOG 0162: A Phase III Randomized Trial of Cisplatin with Paclitaxel Administered by Either 24 Hour Infusion or 96 Hour Infusion in Patients with Selected Stage III & Stage IV Epithelial Ovarian Cancer	455
Potter ME #97/030	O	GOG 0163: A Randomized Study of Doxorubicin Plus Cisplatin Versus Doxorubicin Plus 24-Hour Paclitaxel Plus G-CSF in Patients with Primary Stage III & IV or Recurrent Endometrial Carcinoma	456
Potter ME #97/103	O	GOG 0164: A Randomized, Controlled Intergroup Trial of Salvage Therapy with Paclitaxel and Carboplatin versus Salvage Therapy with Stem Cell Supported High-Dose Carboplatin, Mitoxantrone, and ....	457
Potter ME #95/030	T	GOG 9303, Cisplatin-DNA Adducts in Ovarian Cancer as a Predictor of Response to Platinum-based Chemotherapy.	458
<b>National Surgical Adjuvant Breast &amp; Bowel Project</b>			<b>459</b>
Rearden TP #93/147	O	NSABP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum	460

PI and No.	Status	Title	Page
<b>Pediatric Oncology Group</b>			<b>461</b>
Palmer SR #96/145	O	POG 0942: A Study of Minimally Invasive Surgery of the Chest in Children with Solid Tumors, A Phase III Intergroup Study	462
Palmer SR #93/141	O	POG 8650: Intergroup National Wilms' Tumor Study - 4	463
Palmer SR #95/052	O	POG 8930: A Comprehensive Genetic Analysis of Brain Tumors	464
Palmer SR #95/018	O	POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation	465
Palmer SR #93/164	O	POG 9047: Neuroblastoma Biology Protocol	466
Palmer SR #95/008	O	POG 9153: Intergroup Rhabdomyosarcoma Study/Laboratory Evaluation of Tumor Tissue	467
Palmer SR #95/084	O	POG 9182: HIV/Malignancy Biology Protocol	468
Palmer SR #95/056	O	POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study	469
Palmer SR #94/033	O	POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study	470
Palmer SR #93/148	O	POG 9233/34: A Phase III Randomized Trial of standard vs Dose-Intensified Chemotherapy for Children Less Than 3 Years of Age With A CNS Malignancy Treated With or Without Radiation Therapy	471
Palmer SR #96/096	O	POG 9315: A Phase III Study of Large Cell Lymphomas in Children and Adolescents	472
Palmer SR #94/072	O	POG 9317: Chemotherapy for Children with Advanced Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B Cell ALL	473
Palmer SR #95/168	O	POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study	474
Palmer SR #94/092	O	POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for .....Osteogenic Sarcoma	475
Palmer SR #95/086	O	POG 9354: A Randomized Phase III Evaluation of Intensified Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide in the Treatment of Newly-Diagnosed Ewing's Sarcoma or Primitive ....	476
Palmer SR #95/087	O	POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies	477

PI and No.	Status	Title	Page
Palmer SR #95/088	O	POG 9382: Molecular Studies of t(11	478
Palmer SR #95/058	O	POG 9400: ALinC 16 Classification (C) Protocol	479
Palmer SR #96/144	O	POG 9404: T-Cell #4 Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced Stage Lymphoblastic Non-Hodgkin's Lymphoma	480
Palmer SR #95/059	O	POG 9405: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)	481
Palmer SR #95/060	O	POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)	482
Palmer SR #96/072	C	POG 9411: SIMAL 9: Treatment of Relapsed Non-T, Non-B Acute Lymphoblastic Leukemia with Intensive Chemotherapy	484
Palmer SR #95/089	O	POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML	485
Palmer SR #97/071	O	POG 9425: Advanced Stage Hodgkin's Disease, A Pog Phase III Study	486
Palmer SR #97/054	O	POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard	487
Palmer SR #96/097	O	POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study	488
Palmer SR #95/186	C	POG 9450: Etoposide/Ifosfamide + G-CSF in the Treatment of Newly Diagnosed Metastatic Osteosarcoma or Unresectable Osteosarcoma	489
Palmer SR #96/039	O	POG 9457: Intensive Therapy with Growth Factor Support for Patients with Ewing's Tumor Metastatic at Diagnosis	490
Palmer SR #96/143	O	POG 9485: Intergroup Protocol, Assessment of the Role of Minimal Access Surgery in the Treatment of Childhood Cancer: Intergroup Laparoscopy Protocol	491
Palmer SR #96/035	O	POG 9490: Topotecan Followed by Multimodal, Multiagent Therapy for Children and Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study	492
Palmer SR #95/015	O	POG 9150/CCSG 6901 - Intergroup Rhabdomyosarcoma Study-IV for Stage I Disease.	493
Palmer SR #95/016	O	POG 9151/CCSG 6902 - Intergroup Rhabdomyosarcoma Study-IV for Stage II and Stage III Diseases.	494

PI and No.	Status	Title	Page
Palmer SR #97/089	O	POG 9553: A Phase II of Neoadjuvant Vincristine, Ifosfamide, Doxorubicin, and G-CSF in Children with Advanced Stage Non-rhabdomyosarcoma Soft Tissue Sarcomas	495
Palmer SR #96/120	O	POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)	496
Palmer SR #97/088	O	POG A9961: A Phse III Prospective Randomized Study of Craniospinal Radiotherapy Followed by one of Two Adjuvant Chemotherapy Regimens (CCNU, CDDP, VCR, or CPM, CDDP, VCR) in Children with Newly-....	497
Palmer SR #97/090	O	POG D9501: Topotecan and Cyclophosphamide, Followed by Multimodel, Multiagent Therapy for Children & Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study	498
Palmer SR #97/145	O	POG D9602: Actinomycin D and Vincristine with or without Radiation Therapy for Newly Diagnosed Patients with Low-Risk Rhabdomyosarcoma or Undifferentiated Sarcoma: An IRS-V Protocol	499
<b>Radiological Diagnostic Oncology Group</b>			<b>500</b>
Smith DV #95/136	O	RDOG(5) 6881: Stereotactic Fine Needle Aspiration Biopsy and Core Needle Biopsy in the Work-up of Lesions Detected by Mammography	501
<b>Southwest Oncology Group</b>			<b>502</b>
Davidson H #77/054	O	SWOG 7406: Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III	503
Davidson H #77/053	O	SWOG 7433: Non-Hodgkin's Lymphomas (Stages I, IE, II, and IIE). A Phase III Study.	504
Davidson H #77/024	O	SWOG 7436: Combined Modality Therapy of Breast Cancer	505
Davidson H #77/018	O	SWOG 7510: Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel	506
Davidson H #78/002	O	SWOG 7713/14: Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance After Remission Induction	507
Davidson H #78/047	O	SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6	508
Davidson H #79/096	O	SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III	509
Davidson H #81/064	T	SWOG 8027: The Natural History of Pathological Stage T(1-2) N(O), M(O) ER+ Breast Cancer	510



PI and No.	Status	Title	Page
Davidson H #84/018	O	SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer	511
Davidson H #85/076	O	SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II	512
Davidson H #83/056	O	SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study	513
Davidson H #84/059	O	SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III	514
Davidson H #85/009	O	SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II	515
Sowray PC #86/007	O	SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III	516
Davidson H #87/033	T	SWOG 8501 (INT 0051): Intraperitoneal Cis-platinum/IV Cyclophosphamide vs IV cis-platinum/IV Cyclophosphamide in Patients with Non-measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III ....	517
Davidson H #87/107	O	SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III	518
Davidson H #86/080	O	SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma	519
Davidson H #85/073	O	SWOG 8590: Phase III Study to Determine the Effect of Combining Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of the Head and Neck, Phase III (Intergroup Group.....	520
Davidson H #85/064	T	SWOG 8591: NCI Intergroup #0035, An Evaluation of Levamisole Alone or Levamisole plus 5-Fluorouracil as Surgical Adjuvant Treatment for Resectable Adenocarcinoma of the Colon, Phase III - Intergroup	521
Sowray PC #87/045	O	SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia	522
Davis RC #90/039	O	SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)	523

PI and No.	Status	Title	Page
Davidson H #88/065	O	SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy	524
Davidson H #88/076	O	SWOG 8738: Treatment of Extensive Non-small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III	525
Sowray PC #90/063	T	SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors	526
Thrasher JB #94/119	O	SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy	527
Davidson H #88/066	O	SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)	528
Sowray PC #90/064	O	SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas	529
Davidson H #89/080	O	SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast....	530
Sowray PC #91/020	T	SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II	531
Sowray PC #91/087	O	SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol	532
Davidson H #90/027	O	SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary....	533
Davidson H #90/047	O	SWOG 8854: prognostic Value of Cytometry Measurements of Breast Cancer DNA from Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814	534
Gomez PL #91/067	O	SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients	535
Gomez PL #90/055	O	SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III	536

PI and No.	Status	Title	Page
Davidson H #90/029	O	SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History...	537
Davidson H #89/021	O	SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin + 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in...	538
Stapleton LM #91/089	O	SWOG 8947: Central Lymphoma Serum Repository Protocol	539
Gomez PL #91/007	O	SWOG 8957: Feasibility Trial of Post-Operative Radiotherapy Plus Cisplatin Followed by Three Courses of 5-FU Plus Cisplatin in Patients with Resected Head and Neck Cancer, Phase II Pilot	540
Phillips WA #91/021	C	SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver	541
Thrasher JB #94/131	C	SWOG 8994: Evaluation of Quality of Life in Patients with Stage C Adenocarcinoma of the Prostate Enrolled on SWOG 8794	542
Davidson H #90/056	O	SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide	543
Davidson H #93/056	O	SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients	544
Bertram KA #91/094	O	SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary	545
Stapleton LM #92/051	O	SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II	546
Sowray PC #91/033	O	SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for ....	547
Gomez PL #93/143	O	SWOG 9019: A Phase III, Randomized, Prospective Comparison Between Chemotherapy Plus Radiotherapy, and the Same Chemotherapy Plus Radiotherapy Together With Surgery for .... Non-Small Cell Lung Cancer	548
Bertram KA #92/052	O	SWOG 9031: A Double Blind Placebo Controlled Trial of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Leukemia, Phase III	549

PI and No.	Status	Title	Page
Bertram KA #92/095	O	SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia	550
Williams RF #95/062	O	SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III	551
Davidson H #91/069	O	SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study	552
Rearden TP #94/104	O	SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.	553
Hu JSD #97/096	O	SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-FU....	554
Rearden TP #93/032	O	SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation....Breast Cancer at High Risk of Recurrence	555
Thrasher JB #94/095	C	SWOG 9109: Neoadjuvant Zoladex and Flutamide in Bulky and Non-Bulky Clinical Stage C Carcinoma of the Prostate, Phase II	557
Sowray PC #92/053	O	SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II	558
Gomez PL #92/017	O	SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma	559
Robson ME #93/154	O	SWOG 9126: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in High Risk Acute Myelogenous Leukemia, Phase III	560
Robson ME #94/097	O	SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III	561
Sowray PC #92/056	O	SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients	562
Sowray PC #92/054	C	SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II	563
Rearden TP #93/042	C	SWOG 9152 (EST-4890): Prediction of Recurrence and Therapy Response in Patients with Advanced Germ Cell Tumors by DNA Flow Cytometry	564

PI and No.	Status	Title	Page
Hu JSD #97/042	O	SWOG 9201 (RTOG 91-11): Phase III Trial to Preserve the Larynx: Induction Chemotherapy and Radiation Therapy versus Concomitant Chemotherapy and Radiation Therapy Versus Radiation	565
Sheffler RL #93/097	O	SWOG 9205: Central Prostate Cancer Serum Repository Protocol	566
Hu JSD #94/115	O	SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133	567
Hu JSD #93/107	O	SWOG 9210: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD-P to VAD-P/Quinine for Induction	568
Thrasher JB #94/010	O	SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup	569
Hu JSD #95/023	O	SWOG 9219: A Phase II Evaluation of Interleukin-4 (IL-4) in Patients With Non-Hodgkin's Lymphoma or Hodgkin's Disease	570
Vallion RD #93/136	O	SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer	571
Hu JSD #93/108	O	SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma	572
Robson ME #93/092	O	SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease	573
Ellis RB #94/161	O	SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer	574
Rearden TP #94/105	C	SWOG 9252: Prospective Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II and Stage IIIa Non-small Cell Lung Cancer, Intergroup	575
Robson ME #94/073	O	SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea.... Diagnosed Chornic Myelogenous Leukemia in Chronic Phase	576
Rearden TP #93/166	O	SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer	577
Rearden TP #94/111	O	SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + ...	578

PI and No.	Status	Title	Page
Ellis RB #94/106	C	SWOG 9308: Randomized Trial Comparing Cisplatin With Cisplatin Plus Intravenous Navelbine in the Treatment of Previously Untreated, Stage IV Non-small Cell Lung Cancer Patients	579
Ellis RB #94/170	O	SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast.... 0-3 Positive Nodes	580
Hu JSD #94/107	O	SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phse III	581
Rearden TP #94/114	C	SWOG 9323: Laboratory/Clinical Correlative Studies in Non-Small Cell Lung Cancer: Ancillary Study to SWOG 9252 (INT-0115, E3590, RTOG 91-05, NCCTG 91-24-51)	582
Hu JSD #96/116	O	SWOG 9327: Randomized Phase II Pilot Study of Pentoxifylline (Trental) and Placebo in Patients with Metastatic Malignancy and Anorexia/Cachexia Syndrome	583
Rearden TP #94/058	O	SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary	584
Hu JSD #95/147	O	SWOG 9333: A Randomized Controlled Trial of Mitoxantrone & Etoposide vs Daunomycin & Cytosine Arabinoside as Induction Therapy in Patients Over Age 55 with Previously Untreated Acute Myeloid Leukemia	585
Vallion RD #94/121	O	SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell...	586
Willadsen DS #95/091	C	SWOG 9340: A Phase III Randomized Study of Radiotherapy With or Without BUdR Plus Procarbazine, CCNU, and Vincristine (PCV) for theTreatment of Anaplastic Astrocytomasma	587
Hu JSD #96/012	O	SWOG 9347: Phase III Comparison of Tamoxifen versus Tamoxifen with Ovarian Ablation in Premenopausal Women with Axillary Node-Negative Receptor-Positive Breast Cancer < 3cm, Intergroup	588
Hu JSD #95/024	O	SWOG 9349: A Randomized Phase II Trial of CHOP with G-CSF Support or ProMACE-CytaBOM With G-CSF Support for Treatment of Non-Hodgkin's Lymphoma	589
Rearden TP #95/003	O	SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer	590

PI and No.	Status	Title	Page
Willadsen DS #95/093	O	SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas	591
Ellis RB #94/163	O	SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study	592
Rearden TP #95/094	O	SWOG 9415: Phase III Randomized Trial of 5-FU/Leucovorin/Levamisole versus 5-FU Continuous Infusion Levamisole as Adjuvant Therapy for High-Risk Resectable Colon Cancer, Intergroup	593
Hu JSD #95/151	O	SWOG 9416: A Phase II Intergroup Trial of Induction Chemoradiotherapy Followed by Surgical Resection for Non-Small Cell Lung Cancer Involving the Superior Sulcus (Pancoast Tumors)	594
Hu JSD #97/134	O	SWOG 9419: Tumor Tissue Biopsy for Thymidylate Synthase Expression in Patients with Colorectal Cancer, Ancillary	595
Hu JSD #97/006	O	SWOG 9420: A Phase III Trial of Continuous Low-Dose Infusion Versus Intermittent High-Dose Infusion of 5-Fluorouracil in Patients with Disseminated Colorectal Cancer	596
Hu JSD #96/102	O	SWOG 9445: Prognostic Factor Panel to Predict Preferred Therapy for Node Positive Postmenopausal Breast Cancer Patients (CAF vs Tamoxifen) (A Companion Protocol to SWOG 8814)	597
Caton JR #96/094	O	SWOG 9446: Chemoprevention Trial to Prevent Second Primary Tumors with Low-Dose 13-Cis Retinoic Acid in Head and Neck Cancer	598
Hu JSD #96/117	C	SWOG 9449: Phase II Study of VIP (Etoposide, Ifosfamide and Cisplatin) in the Treatment of Invasive Thymoma	599
Hu JSD #97/009	O	SWOG 9457: Paclitaxel (Taxol) and Carboplatin for Advanced Transitional Cell Carcinoma of the Urothelium	600
Hu JSD #97/059	O	SWOG 9503 (NCCTG 93-72-52): Phase III Trial of BCNU and Cisplatin Versus BCNU Alone and Standard Radiation Therapy Versus Accelerated Radiation Therapy in Patients with Grade 4 Glioma	601
Hu JSD #96/147	O	SWOG 9509: A Randomized Phase III Trial of Paclitaxel Plus Carboplatin Versus Vinorelbine and Cisplatin in Untreated Advanced Non-Small Cell Lung Cancer	602
Hu JSD #97/041	O	SWOG 9510: Evaluation of Topotecan in Hormone Refractory Prostate Cancer, Phase II	603

PI and No.	Status	Title	Page
Hu JSD #96/095	O	SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary..	604
Hu JSD #96/118	O	SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck	605
Hu JSD #97/005	O	SWOG 9518: Phase II Trial of Continuous Topotecan Infusion in Patients with Advanced Soft Tissue Sarcomas	606
Hu JSD #96/160	S	SWOG 9519: Evaluation of Tomudex in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck	607
Hu JSD #96/119	S	SWOG 9520: Controlled Phase II Study of Doxorubicin and Paclitaxel as Frontline Chemotherapy for Women With Metastatic Breast Cancer	608
Hu JSD #97/070	O	SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour ....	609
<b>University of Washington Neuro-Oncology Group</b>			<b>610</b>
Davidson H #89/013	O	UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System	611



**INTENTIONALLY LEFT BLANK**

# DETAIL SHEETS FOR PROTOCOLS

62ND MEDICAL GROUP

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/143		<b>Status:</b> Completed	
<b>Title:</b> Training of Veterinary Food Inspection Personnel in Field Slaughter and Inspection Methods Utilizing Domestic Swine (Sus scrofa domesticus)					
<b>Start Date:</b> 05/26/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> 62nd Medical Group			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> C. H. Martinez					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Training:food inspection,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To train veterinary food inspection personnel in antemortem and postmortem inspection, dispatch, and field slaughter techniques.

**Technical Approach:** This training protocol will provide experience for food inspection personnel on techniques used within their occupation. A total of two domestic pigs will be used over a 6 month period. After being transported to the training area, the pigs will be inspected using recommended antemortum techniques, stunned using a captive bolt device or mallet and immediately exsanguinated. The methods used are approved by the AVMA Panel on Euthanasia and cause minimal pain or distress to the animals. The pigs will then be eviscerated and inspected using recommended postmortem techniques.

**Progress:** One session was held using one pig in FY 97.

**DETAIL SHEETS FOR PROTOCOLS**

**FORT LEWIS, SPECIAL FORCES**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/069		<b>Status:</b> Completed
<b>Title:</b> Special Operations Medical NCO Sustainment Training				
<b>Start Date:</b> 03/04/94		<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Special Forces		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Charles Taylor, MC				
<b>Associate Investigators:</b> CPT G. Jeffrey Poffenbarger, MC		Games J		
<b>Key Words:</b> Training, medical, special operations,Animal Study				
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b> 12/19/96
	\$0		\$0.00	

**Study Objective:** To support required annual Advanced Trauma Life Support type surgical training for all 18D Special Forces medical sergeants. To have exposure, gain experience, and develop proficiency in surgical procedures.

**Technical Approach:** The following surgical procedures will be performed: Endotracheal intubation, vessel cutdown and catheterization, Soft tissue handling/suturing, chest tube insertion, cricothyroidotomy, pericardiocentesis. All procedures will use goats and support staff from the Department of Clinical Investigation's Laboratory Animal Surgery Service. The trainees will be evaluated through visual observation of satisfactory skill level. Additionally, there will be a 2 day didactic course prior to the animal lab, which will culminate in a written test. After the animal lab all students will undergo a 20 minute oral exam on their performance and details of trauma medicine.

**Progress:** Three training sessions using 12 animals were held in FY 97. The protocol was terminated due to the expiration of the three-year approval limit. It was replaced by MAMC #97/117, Jul 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/117		<b>Status:</b> On-going
<b>Title:</b> Special Operations Medical NCO Sustainment Training Using the Goat Model (Capra hircus)				
<b>Start Date:</b> 07/18/97		<b>Est. Completion Date:</b> Jul 00		
<b>Department:</b> Special Forces		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Charles Taylor, MC				
<b>Associate Investigators:</b> SFC Paul Linskens		2LT David Nieman, PA-C, MS-SP		
<b>Key Words:</b> Special Operations Training, goat model,Animal Study				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: Ranger medical personnel will be exposed, gain experience and demonstrate proficiency in the following invasive resuscitation procedures: cricothyroidotomy (needle and surgical), endotracheal intubation, needle thoracentesis, chest tube placement, pericardiocentesis, intravenous catheterization, venous cutdown and techniques of suture placement.

Technical Approach: Anesthetized adult goats will be used to train Ranger medical personnel basic surgical and emergency resuscitation skills they are expected to perform in combat. These tasks are identified by the American College of Surgeons in the Advanced Trauma Life Saving course. Ranger medical personnel must achieve a score of 70% on the written exam at the conclusion of the didactic instruction before proceeding to the hands on portions of the exercise. This protocol does not vary from previously accepted regimens for this purpose.

Progress: This study replaced MAMC #94/069 in July 1997. One training session was held in Aug 97 which used 12 animals.

**DETAIL SHEETS FOR PROTOCOLS**

**UNITED STATES  
DEPARTMENT OF AGRICULTURE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 92/001		<b>Status:</b> On-going
<b>Title:</b> Methods for Assessing Vitamin A Status in Healthy Adults				
<b>Start Date:</b> 10/04/91		<b>Est. Completion Date:</b> Jul 92		
<b>Department:</b> USDA		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Betty Jo Burri, Ph.D.				
<b>Associate Investigators:</b>		Andrew J. Clifford, Ph.D.		
<b>Key Words:</b> liver,vitamin A,isotope technique				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** To determine vitamin A status in healthy free-living adults in the San Francisco area.

**Technical Approach:** This protocol will consist of studies focusing on three groups of people: (1) women aged 55-60 (2) men aged 55-60 and (3) men aged 18-24. Each group will consist of 30 healthy nonsmokers. These age and sex groups have been selected to include adults with divergent ages and because vitamin A and its analogs can be teratogenic, making it potentially hazardous to administer analogs to young women. Subjects will be prescreened for serum retinol and holo-retinol binding protein (RBP) in an effort to get at least 15 people in each group with low vitamin A serum concentrations. Subjects will fill out a questionnaire in order to estimate their usual intake of high vitamin A foods over the past year. Body weights and blood pressures will be measured on the first and last days of the study. The vitamin A analogs are to be given on days one (didehydroretinol) and eight (tetradeuterated retinol acetate) of the study. In a pilot study to test the time course of equilibration and elimination of the analogs, three volunteers from each group will be given the cocktails as stated and blood samples taken at 5, 8, and 30 hrs, and at 2, 3, 4, 5, 15 days and every 30 days thereafter. This blood would be collected in addition to the blood required for the regular study (pre ingestion, 5 hr, and days 8, 29, and 30). The study will compare three promising new methods for assessing vitamin A status to serum retinol, and to vitamin A liver stores measured by deuterated analogs and by vitamin A2. The new methods tested will be free- and transthyretin-bound holo-retinol binding protein as determined by HPLC, erythrocyte transglutaminase levels, and goblet cell abnormalities. Addendum (Oct 91): All of the testing was done except for tests of the vitamin A2. Vitamin A2 proved to be very difficult to purify, so it was never actually given to the subjects. Then two significant things happened; a supply of high quality vitamin A2, approved for human use, was obtained, and it was found that the tetradeuterated analog may interfere with the vitamin A2 test, even when these analogs are given 8 days apart. It is now recommended that the doses of vitamin A2 and other analogs be separated by at least 30 days. Therefore in this study, the vitamin cocktails will be given on day 1 and day 30, with blood draws added as appropriate.

**Progress:** This is a longitudinal study in which 54 patients were entered in previous years. They are due for follow-up in late 1997.



**DETAIL SHEETS FOR PROTOCOLS**

**ANESTHESIA & OPERATIVE SERVICES**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/042	<b>Status:</b> Terminated
<b>Title:</b> Prolonged Analgesia Using Microencapsulated Morphine in A Mouse Model (Mus musculus)		
<b>Start Date:</b> 01/19/96	<b>Est. Completion Date:</b>	
<b>Department:</b> Anesthesia & Operative Services	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Benjamin J. Miller, MC		
<b>Associate Investigators:</b> MAJ Stephen L. Bolt, MC		
<b>MAJ James D. Helman, MC</b>		
<b>Key Words:</b> Morphine:microencapsulated, mouse model,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Sudy Objectives: To determine if microencapsulated morphine, injected intraperitoneally in mice, will produce a sustained analgesic effect using a tail flick test.

Technical Approach: This study will include six separate experiments and will utilize a total of 26 mice. (1) Determination of base line Tail flick latencies. (2) Determination of LD50 of Intraperitoneal injections of plain morphine. (3) Determination of LD50 of IP injected morphine loaded microspheres. (4) Tail flick latency tests with plain morphine. (5) Tail flick latency tests with empty microspheres. (6) Tail flick latency test with morphine loaded microspheres.

Progress: This protocol was not started due to the reassignment of the principal investigator. Other staff in the Department of Anesthesia were not interested in pursuing the study.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF  
CLINICAL INVESTIGATION**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/103		<b>Status:</b> Terminated	
<b>Title:</b> Polymerase Chain Reaction Detection and Cell Culture of Herpes Simplex Virus from Urine of Symptomatic Males with Non-gonococcal Urethritis					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Oct 95		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS					
<b>Associate Investigators:</b> MAJ Darrell E. Griffin III, MS			LTC Margot R. Krauss, MC		
<b>Key Words:</b> Herpes simplex, polymerase, non-gonococcal urethritis					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To determine the feasibility of using a urine sample for detection and culture of Herpes Simplex Virus (HSV) in patients suspected of having non-gonococcal urethritis (NGU) due to HSV.

**Technical Approach:** Twenty males presenting with HSV And NGU will be tested for evidence of HSV infection in the urethra. Urine will be submitted from the Dept. of Pathology to the Dept. of Clinical Investigation for analysis. Cells will be collected from the urine by centrifugation and processed for cell culture and for detection by the polymerase chain reaction (PCR) using primers specific for HSV. Results of cell culture will be compared with PCR results. Samples positive for both culture and PCR will be considered true positives and thus will determine the feasibility of using urine samples for HSV detection in NGU patients. This is a descriptive study of a new technique.

**Progress:** This protocol has been terminated due to an inability to enroll a sufficient number of patients for valid conclusions. Eleven patients were entered (all previous to FY 97) with no adverse reactions.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/025	<b>Status:</b> On-going
<b>Title:</b> The Department of Clinical Investigation's Molecular Biology Short Course for Physicians		
<b>Start Date:</b> 01/20/95	<b>Est. Completion Date:</b> Jun 96	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS OMA Cost:		
<b>Associate Investigators:</b> MAJ Rodger K. Martin, MS CPT Aziz N. Qabar, MS		
<b>Key Words:</b> Molecular biology, training course		
\$0.00		<b>Periodic Review:</b> 9/30/97

**Study Objective:** To familiarize MAMC residents, fellows, and staff physicians with the research capabilities and resources of the Department of Clinical Investigation. To support MAMC Graduate Medical Education through instruction and research. To foster an appreciation of molecular biology concepts in residents, fellows, and staff physicians and to augment their understanding of the scientific literature. To encourage residents, fellows and staff physicians to develop research protocols incorporating these technologies.

**Technical Approach:** This course is designed to familiarize physicians with the most commonly encountered molecular approaches in the scientific and clinical literature. It is hoped that this will foster more critical reading of the literature as well as encouraging the development of research protocols employing these technologies. Although six weeks in duration, students will be required to attend two hours of lecture per week in addition to approximately seven hours of laboratory exercises. Topics addressed and used in the course range from DNA isolation to cloning and sequencing of PCR products.

**Progress:** 21 people took the course during FY 97. A workshop was presented at the SAFMLS annual meeting in Spokane, WA.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/058		<b>Status:</b> On-going
<b>Title:</b> Detection of Telomerase Activity from Plasmodium falciparum				
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS				
<b>Associate Investigators:</b> MAJ Curtis L. Yeager, MS			MAJ Rodger K. Martin, MS MAJ Dennis E. Kyle, MS	
<b>Key Words:</b> Telomerase, Plasmodium falciparum, DNA				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** (1) To modify and to optimize the telomerase repeat amplification protocol (TRAP) employing nonradioactive methods for detection of telomerase activity from the human parasite, *P. falciparum*. (2) To develop DNA primers specific for *P. falciparum* telomerase. (3) To detect and to identify by the modified TRAP assay *P. falciparum* telomerase activity.

**Technical Approach:** Total protein extractions from normal human testis tissue, erythrocytes, and *Plasmodium falciparum* will be performed. Parasites will be harvested from in vitro cultures and protein concentrations will be measured. TRAP assays will be performed as described with modifications. PCR amplification of the TRAP assay will be performed. Standard TRAP assays will also be performed. TRAP PCR products will be analyzed on 10% non-denaturing gels. TRAP assays will be performed with a fluorescein-labeled forward TS primer for *P. falciparum*. Data will be generated in fluoregram and chromatogram forms. TRAP assay products will be amplified using the GeneAmp PCR Reagent Kit and will be visualized by ethidium staining in 12% Tris-Glycine acrylamide gels. Standard procedures for DNA hybridization will be performed using the amplified TRAP products. TRAP amplification products will be analyzed by electrophoresis on a 4% agarose gel, visualized by ethidium bromide and UV irradiation. Bands representative of telomeric repeats will be excised from the gel. Purified DNA will be cloned and ligation mixes will be used for transformation into competent cells. Sequencing of repeats will be accomplished and detected with ALF DNA analysis.

**Progress:** We first proved that telomerase is present in asynchronous erythrocytic cultures of *Plasmodium falciparum*, and next decided to see if enzyme activity is stage specific according to the 3 main stages in the erythrocytic life cycle. Next we looked at various compounds for their ability to inhibit telomerase activity at these same stages. A couple of compounds appear to show promise as therapeutic agents, but further studies will be warranted to prove their efficacy.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/162	<b>Status:</b> Completed
<b>Title:</b> Indirect Quantitation of Telomerase Activity		
<b>Start Date:</b> 09/20/96	<b>Est. Completion Date:</b> Aug 97	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Wade K. Aldous, MS		
<b>Associate Investigators:</b> M. J. Styner, B.S. Morgan E. Shook		
<b>Key Words:</b> Proteins, telomerase		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** 1) To utilize the F-TRAP assay, the reverse transcriptase assay, the telomerase ELISA, and the TRAPeze methods to determine if any methods produce linear relationships with serially diluted extracts; 2) to pick the best method above based upon reliability, cost, ease of use, and time of use; and 3) to assay several different extracts with controls to find ranges of high and low activity in comparison with tumor specificity and staging.

**Technical Approach:** A previously extracted protein sample will be subjected to the 4 different methods outlined above in search of the optimal test. The best-test will be used to assay several other protein extracts in order to find ranges of enzyme activity. Values derived from the different extracts will be compared to each other based on tumor specificity and staging.

**Progress:** The original method in the Department of Clinical Investigation was evaluated against some newer kits to determine the best method according to cost, sensitivity, ease of use, and reliability. Although the original method was most sensitive, the high cost of the equipment precludes many from performing the same assay. One of the kits, which uses an ELISA format to detect telomerase activity and quantitate it, was outstanding, and will be used for telomerase expression in the future.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/031		<b>Status:</b> Terminated	
<b>Title:</b> Introduction of Fundulus gardneri as A Bioassay Model for Carcinogenicity and Toxicological Testing					
<b>Start Date:</b> 12/19/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> SGT George W. Heath, NC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Carcinogenicity, Toxicology, bioassay, Fundulus gardneri,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>9/30/97</b>

Study Objective: 1) To introduce and establish *F. gardneri* as an economical and viable species to the biomedical research community as a bioassay model for carcinogenicity and toxicological testing. 2) To induce hepatic degeneration with various dosages of diethylnitrosamine and to test the effects of exposure level on the severity and types of lesions and neoplasms that will be seen.

Technical Approach: 70 pairs of *Fundulus gardneri* will be utilized to produce offspring that will be raised and exposed to a known carcinogen at two weeks of age (with exception of control group). Each pair can be expected to produce at least 1 dozen viable offspring in this short period of time. This protocol will require each pair to produce 7.5 offspring, well within expectations for a total of 525 viable fry. These will be known as F1 Groups 1-5. After exposures liver and other tissues will be harvested at 4, 8, 12, 16 and 24 weeks post exposures and histologically evaluated for hepatocellular generation and necrosis. All animals will be sacrificed at time of harvesting. The carcinogen used will be diethylnitrosamine at the following dose for a period of 48 hrs:

Group 1	Group 2	Group 3	Group 4	Group 5
100 mg/L	200 mg/L	400 mg/L	500 mg/L	Control

Each F1-Group will consist of 75 fish that will be housed separately in filtered 20-gallon aquariums from the time they are hatched to 24 weeks of age. At two weeks of age each experimental group, with the exception of Group 5 (control), will be transferred to exposure tank for a period of 48 hrs during which time they will be exposed to diethylnitrosamine for 48 hrs. They will then be returned to their conventional tank for standard rearing procedures. After initial exposure 10% of each group will be sacrificed and histologically evaluated for hepatic necrosis at four-week intervals for the first 16 weeks and then eight weeks later for final evaluation. Group 6 and 7 will be individually housed in two 20-gallon tanks for species maintenance and documentation.

Progress: Twenty-five 10 day old *Fundulus gardneri* were exposed to 500 mcg/l dimethylnitrosamine (a known carcinogen) for 48 hours. Hepatic and histological evaluations were performed at 30 and 60 days. Fish that were exposed to the carcinogen exhibited profound skeletal abnormalities, including bent, S-shaped spinal columns. The total number of fish that we planned to use could not be raised due to a microscopic parasite that infected the incubating fish eggs. This parasite was photographed and the photographs reviewed by a Veterinary Pathologist.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/169		<b>Status:</b> Terminated	
<b>Title:</b> Development of a Method to Study What Proteins Are Regulated by IGF in the PC3 Prostate Cancer Cell Line Using 2-D Gel Electrophoresis and Protein Sequencing					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Louis A. Matej, B.S.					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:prostate, cell line, protein regulation, IGF					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** The objective of this study is to develop a method for using a 2-D Electrophoresis coupled with Protein Sequencing to quantitate and identify proteins produced or inhibited by PC3 Prostate Cancer Cells when regulated by IGF.

**Technical Approach:** PC3 prostate cancer cells will be grown to confluency at 37°C in RPMI media supplemented with 5% Fetal Bovine Serum and in a 6% humidified CO<sub>2</sub> atmosphere. One culture will be inoculated with IGF at 10<sup>-6</sup>M; another culture will serve as a normal control. In the media of both the regulated and non-regulated PC3 prostate cell cultures, C<sup>14</sup> labeled amino acids will be added to allow in the detection of proteins by autoradiography. The cultures will be allowed to incubate for 48 hours. The media will be pipetted and saved to further study extracellular proteins while the cells will be trypsinized, sonicated in lysing buffer, and the mixture ultracentrifuged to acquire intracellular proteins for further study. The investigator plans to isolate and wash the protein from these solutions by using a dot blot apparatus to bind proteins to a nitrocellulose membrane. The proteins can then be desalted and washed on the membrane. To extract the proteins off the nitrocellulose membrane, we will use 8 M urea in sample buffer. The IEF (1st dimension) electrophoresis which separates protein by isoelectric point will be carried out using polyacrylamide tube gels having equal amounts of ampholyte pH range 4.0-6.0, ampholyte pH range 6.0-8.0 and ampholyte pH range 7.0-9.0. The second dimension electrophoresis will be carried out by layering the tube gel onto a vertical 10 to 20 percent gradient polyacrylamide gel. The investigator will transfer the proteins onto a PVDF membrane by using an electroblot apparatus followed by staining with coomassie blue and destaining with a methanol/acetic acid/water solution. Autoradiography will then be used to allow more sensitive identification of protein bound to the PVDF membrane. After visual, graphic, and computer analysis of the autoradiographs, purified protein spots will then be cut out of the membrane and sequenced using the ABI protein sequencer. The protein sequences will be used to compare quantities of each protein of interest as well as for identification.

**Progress:** No samples were collected. The 2D electrophoresis equipment required for consistent was not purchased. The present 2D system is inadequate for repeated pouring of consistent gradient gels.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 90/091		<b>Status:</b> On-going	
<b>Title:</b> A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp(6)-Des-Gly(10)-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing....					
<b>Start Date:</b> 07/20/90			<b>Est. Completion Date:</b> Nov 92		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Donald R. McClellan, MC					
<b>Associate Investigators:</b>			COL Dan C. Moore, MC		
<b>Key Words:</b> precocious puberty,deslorelin,LH					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		07/18/97	

Study Objective: To treat patients who have central precocious puberty with Deslorelin in order to suppress pubertal development and excess growth, to restore gonadotropin and sex hormone levels to normal prepubertal levels, and to demonstrate the safety of such treatment.

Technical Approach: Central precocious puberty will be defined as: stage 2 pubic hair or greater, stage 2 breast or genital development or greater, pubertal LH and FSH peak following GnRH stimulation, and absence of peripheral origin of precocity (lack of adrenal or ovarian mass on ultrasound and normal serum hCG). After diagnosis and standard evaluations, patients will be given Deslorelin, 4 mcg/kg SC daily. At three month intervals, patients will be re-evaluated. A physical examination with pubertal staging will be done. Serum sex hormones and gonadotropins (pre and post GnRH) will be measured and bone age will be determined. Treatment will be continued until the patient reaches an age at which pubertal development is deemed appropriate (usually 10-11 years) at which time therapy will be discontinued.

Progress: No subjects were entered during FY 97, for a total of 3 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/081		<b>Status:</b> Terminated	
<b>Title:</b> Genentech National Cooperative Growth Study (NCGS) Post Marketing Surveillance Program for Protropin (Somatrem for Injection) and Nutropin (Somatropin [rDHA Origin]) for Injection)					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Dec 04		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Dan C. Moore, MC					
<b>Associate Investigators:</b>			LTC Robert J. Newman, MC		
<b>Key Words:</b> Growth:delay, Protropin, Nutropin					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

Study Objective: To collect long-term safety and efficacy information regarding treatment of children who have growth failure due to a lack of endogenous growth hormone secretion with Protropin and/or Nutropin growth hormone (GH).

Technical Approach: This is a multi-center, open label, post-marketing surveillance study of Protropin and Nutropin in the United States and Canada. Patients are enrolled at the time of their initiation of Protropin or Nutropin therapy and followed throughout their course of therapy. Post-treatment height measurements are collected until adult height is achieved. Since this is a record review and data collection only protocol, the number of patients enrolled will depend on the number requiring treatment for standard medical indications.

Progress: This study was intended to follow growth of children receiving growth hormone produced by Genentech. However, the institution changed to a different manufacturer and no children are taking this product. It is terminated because the principal investigator retired.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/033		<b>Status:</b> Completed	
<b>Title:</b> Localization and Identification of Sex Hormone Binding Globulin (SHBG) mRNA and SHBG-Related Proteins in Breast Cancer (Production of Monoclonal Antibodies Using Mice)					
<b>Start Date:</b> 12/01/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
<b>Key Words:</b> Cancer:breast, SHBG, antibodies,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** (1) To detect the message (mRNA) for sex hormone binding-globulin (SHBG) in breast tissue sections in-situ. (2) To determine if breast cancer cell lines are producing alternate transcripts of SHBG mRNA, and to characterize these transcripts and their protein product.

**Technical Approach:** This will be approached by amplifying the mRNA in the tissue sections by the polymerase chain reaction (PCR), first using reverse transcriptase to make cDNA copies of the mRNA in the section. The primer set that our laboratory is currently using to amplify SHBG message from RNA extracted from formalin fixed tissue will be the initial set used. Two control mRNAs will be evaluated, B-2 microglobin (b2) and porphobilinogen deaminase (PBGD). These mRNAs will be amplified in adjacent sections cut from the breast cancer tissue blocks. The amplified cDNA will be visualized through the inclusion of digoxigenin-11 dUTP (DIG) included in the amplification mix. The DIG labeled PCR fragments will be detected using a alkaline phosphatase reaction. A cDNA library will be constructed from ZR-75-1, MCF-7 and MDA-MB-231 breast cancer cell lines. We will screen the library for clones positive for wild type SHBG sequence and alternate sequence using a 550 bp probe. Next, based on the predicted amino acid sequence of the transcripts, peptides will be synthesized and monoclonal antibodies raised against the peptides from the alternate transcripts. These antibodies will be used to examine conditioned media from breast cancer cell lines and cellular extracts of these cells for the presence of protein produced from SHBG alternate mRNA transcripts.

**Progress:** A cDNA library was produced from MCF-7 breast cancer cells. The library was initially screened by solution hybridization using an oligonucleotide to exon 3 of sex hormone binding globulin. The selected library was subsequently screened with a 500 bp cDNA probe spanning the 5' region of the message. Positive clones are in the process of being subcloned and rescreened. To date, 3 positive clones have been identified. These will be sequenced to determine the complete sequence of SHBG mRNA expressed in breast cancer cells.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/126		<b>Status:</b> On-going	
<b>Title:</b> Sex Hormone Binding Globulin and Prostate Cancer - Characterization of Alternate mRNA Transcripts					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> Louis A. Matej, B.S.			CPT Wade K. Aldous, MS M. J. Styner, B.S.		
<b>Key Words:</b> Cancer:prostate, SEBG, mRNA transcripts					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** 1) To characterize the sex hormone binding globulin (SHBG) mRNA produced by prostate cancer cells. This will be accomplished by characterizing the SHBG products amplified by PCR, and ultimately the full length transcripts. 2) To determine if SHBG mRNA is translated into protein. This will be accomplished by metabolically labeling the proteins in the cells and detecting by immunoprecipitation. A long range objective is to develop an antibody against the protein product of an altered SHBG mRNA, and use this antibody to determine if the proposed altered transcript is translated into functional protein.

**Technical Approach:** We will examine prostate cancer cell lines for the presence of SHBG mRNA. In addition, we will construct a cDNA library to fully characterize the SHBG transcripts produced by prostate cancer cells. We plan to examine the proteins manufactured by prostate cancer cell using immunoprecipitation to determine if the cells are producing SHBG protein. This study will thus characterize a potential oncogene for prostate cancer and lead to a greater understanding of the mechanism of cancer formation. This is a descriptive study. The DNA sequences will be compared with known sequences using MacVector.

**Progress:** Reverse transcriptase-polymerase chain reaction (rtPCR) analysis of total RNA revealed two PCR products which were cloned and sequenced. The smaller band was found to be the product of alternate processing of the mRNA, with exon seven removed and a single base deletion at the start of exon 8. This modification is predicted to produce an altered amino acid sequence in the carboxy tail of the protein, removing the glycosylation sites and producing a truncated protein. We also found that both prostate fibroblast and epithelial cells produce SHBG mRNA.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/033		<b>Status:</b> On-going	
<b>Title:</b> Is BRCA1 Loss of Expression Found in Tumors Others Than Breast and Ovarian Cancer					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b>					
CPT Jerome M. McDonald, MC			MAJ Richard F. Williams, MC		
CPT Sandra L. Carter, MC			MAJ Thomas P. Baker, MC		
			James R. Wright, M.T.		
<b>Key Words:</b> Cancer, BRCA1, expression					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** 1) To determine the prevalence of loss of expression of BRCA1 protein in tumors. We will examine tumors that are linked to increased risk of breast cancer (prostate, breast, ovarian and endometrial cancers) in families as well as tumors that are not associated with an increased risk (lung and kidney). We also will examine colon cancer samples, as this tumor may also be linked to BRCA1 associated cancer. 2) Through the use of two antibodies against BRCA1, we can determine if normal protein is being expressed in the tumors and surrounding normal tissue, or if a truncated protein that may be a product of a mutant BRCA1 allele is being expressed.

**Technical Approach:** This study will lead to an increased understanding of the role of BRCA1 protein in tumorigenesis. BRCA1 is associated with familial breast and ovarian cancer. The gene was identified by loss of heterozygosity studies in families with a high incidence of breast and ovarian cancer. In these families, it has been found that members with a mutant allele for BRCA1 have a much greater risk for developing cancer than the unaffected population. The presumed mechanism of action of BRCA1 in the development of cancer involves the loss of the normal allele which was producing a normal, functional protein. The mutant alleles contain a mutation in the BRCA1 gene, of which 85% produce a truncated protein. It is assumed that the truncated protein is not functional. It also is presumed that the function of BRCA1 is as a DNA binding protein. The basis of this assumption is the presence of a zinc ring domain near the amino terminal end of the protein. The zinc ring domain was identified through amino acid sequence homology and molecular modeling. The zinc ring is a common component of DNA binding proteins. This structure in BRCA1 may be functionally important, as a common mutation that is associated with increased risk, 185delAG, deletes two nucleotides in this region.

The presence of an inherited BRCA1 mutation, which may lead to the production of non-functional protein, is becoming a well accepted risk factor for the development of familial breast and ovarian cancer. However, the role of BRCA1 in tumors other than breast and ovarian is not well understood. We will determine if the loss of BRCA1 protein expression occurs in tumors other than breast and ovarian. If BRCA1 loss can be documented in a variety of tumors, this will add to the importance of BRCA1 loss in the progression of a normal cell to a cancerous one.

**Progress:** We have begun evaluating two antibodies directed against BRCA1. One antibody recognizes the amino terminal region of this large protein, the other the carboxy tail. Different tissue pretreatments have been evaluated, including trypsin digestion and pressure treatment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/128		<b>Status:</b> On-going	
<b>Title:</b> Enhancing the Effectiveness of Tamoxifen Therapy in Breast Cancer					
<b>Start Date:</b> 08/15/97			<b>Est. Completion Date:</b> Oct 00		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Katherine H. Moore, Ph.D.					
<b>Associate Investigators:</b> Neset MJM			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:breast, tamoxifen, SHBG, apoptosis, cell cycle					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** 1) Investigate the mechanism by which SHBG and tamoxifen mediate a reduction in cell number in MCF-7 breast cancer cells *in-vitro* by measuring their effect on both G1 cell cycle arrest and apoptosis, as well as level of expression of factors which mediate apoptosis such as Bcl-2 and Bax; 2) study the regulation of production of endogenous SHBG by estrogen and tamoxifen, as well as agents reported to affect SHBG levels on other systems, such as insulin, prolactin, androgen, and cAMP; and 3) determine the effect of simultaneous treatment of MCF-7 cells with exogenous SHBG and tamoxifen on cell growth and apoptosis.

**Technical Approach:** We will be exploring the novel idea that interaction occurs between two effectors of steroid response in breast cancer cells, tamoxifen and sex hormone binding globulin (SHBG), resulting in a reduction of the rate of cell growth and increasing the rate of cell death. This study may provide the foundation to developing more effective treatment of breast cancer. The inhibitory effect of tamoxifen, a partial antagonist of estrogen action, on cell growth has been well documented. Evidence for an effect of tamoxifen on programmed cell death (apoptosis) has been reported recently. In preliminary studies in our laboratory, tamoxifen decreases the level of the anti-apoptosis factor Bcl-2, and this effect appears to depend on the level of estrogen to which cells are exposed prior to treatment. An inhibitory effect of cAMP on cell growth in response to estrogen has been recently shown by others and confirmed in our laboratory. Additionally, treatment with exogenous SHBG has been shown to increase cAMP levels and inhibit response to estrogen. Our group has demonstrated that SHBG is produced endogenously by MCF-7 breast cancer cells. Interestingly, recent data suggest that serum SHBG levels increase in patients treated with estrogen antagonists, suggesting that antiestrogen agents may regulate SHBG production. A potentially important aspect of this study would be the discovery of a means to increase the inhibitory effect of antiestrogens on breast cancer cell growth and/or cell death by modulation of SHBG levels as addressed in objective 2. If one of these agents is found to modulate SHBG levels, and if SHBG is shown to modulate the inhibitory effect of tamoxifen, a potential means of biologically increasing the effectiveness of breast cancer treatment with antiestrogens could be identified.

**Progress:** We are currently performing phase one of this multipart project. We are using the breast cancer cell line (MCF-7) as our model for tamoxifen treatment, as they undergo apoptosis when cultured in the presence of tamoxifen. We cultured MCF-7 cells with different doses of estrogen, tamoxifen and insulin, counted cells, and extracted total RNA. As expected, estrogen and insulin stimulated cell growth, while tamoxifen inhibited cell growth. SHBG expression was measured by semi-quantitative rtPCR. We found that tamoxifen increased SHBG levels in cells even more than estrogen did, while insulin did not appear to change SHBG expression. To more accurately quantitate SHBG expression, we are currently developing internal RNA standard for SHBG, to allow us to perform competitive rtPCR.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/084		<b>Status:</b> Terminated	
<b>Title:</b> Veterinary Support Personnel and Investigator Training in Animal Care Procedures (Swine <i>Sus scrofa</i> , Goat <i>Capra hircus</i> , Rabbit <i>Oryctolagus cuniculus</i> , Ferret <i>Mustela putorius furo</i> , Rat <i>Rattus ...</i>					
<b>Start Date:</b> 02/09/94			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Ronald E. Nielsen, VC					
<b>Associate Investigators:</b>			CPT Stephen Caldwell, VC		
<b>Key Words:</b> Training:vet techs,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$200.00
			<b>Periodic Review:</b>		9/30/97

Study Objective: 1) To help the DCI technical staff to remain proficient in basic technical skills as well as emergency care procedures that may arise during normal animal care. 2) To teach investigators and technicians the basics of animal restraint and manipulations. 3) To teach DCI technical staff basic surgical skills that will enable them to better assist investigators.

Technical Approach: The DCI technical staff trainees will be instructed in proper handling and restraint techniques used with the Swine *Sus scrofa*, Goat *Capra hircus*, Rabbit *Oryctolagus cuniculus*, Ferret *Mustela putorius furo*, Rat *Rattus norvegicus*, and Mouse *Mus musculus*. Trainees will be taught basic surgical skills, to include endotracheal intubation; blood collection and injections; vessel cutdown and catheterization; soft tissue handling and suturing; anesthetic regimens, and necropsy procedures.

Progress: This study was terminated because the three year approval limit had expired and no other personnel were interested in updating and conducting this study.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 93/052		<b>Status:</b> Terminated	
<b>Title:</b> Intrauterine Growth: Factors That Influence the Relationship Between Gestational Age and Birth Weight, Length, and Head Circumference					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Troy H. Patience, B.S.					
<b>Associate Investigators:</b>			LTC Joanna C. Beachy, MC		
<b>Key Words:</b> intrauterine growth, age, birthweight, length, head circumference					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$1000.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** (1) How does the relationship between gestational age and birth weight, length, and head circumference from data gathered from newborn infants compare with published data? (2) Does the average birth weight, length, head circumference and ponderal index at each gestational age differ from year to year of the study (1981 - 1992)? (3) Do infants from twin/multiple gestation pregnancies in this selected population show the expected growth pattern, that is no alteration in growth until the third trimester? (4) Does the classification of diabetic (gestational versus non-gestational) impact on incidence of large for gestational age infants and on the ponderal index?

**Technical Approach:** This is a retrospective review of data from > 24,000 infants born over an 11 year period. Infants with diagnosed congenital anomalies, chromosomal abnormalities and hydrops fetalis will be excluded.

**Data Analysis:** 1) For evaluation of effect of gestational age on birth weight, length, head circumference and ponderal index, all multiple gestation infants and IDMs will be excluded. Data will be analyzed by non-linear regression to generate curve with 95% confidence levels. Alternatively, mean ( $\pm 2$ ) standard deviations, third and tenth percentile of birth weight, length and head circumference will be calculated for each gestational age. A smoothed curve will then be generated and compared to previously published curves. 2) Data will also be stratified by year and analyzed in a similar fashion, that is birth weight, length and head circumference will be compared at each gestational age yearly from 1981 - 1992. Statistical significance will be evaluated by regression analysis or ANOVA, controlled for gestational age. 3) The birth weight, length, head circumference and ponderal index from infants of multiple gestations will be evaluated as in (1) and compared with the standard curves generated in (1) and published for twin gestations. Evaluation of the ponderal index may indicate when the placental supply is no longer sufficient. 4) The birth weight, length, head circumference and ponderal index from IDM will be handled in a similar manner. Subdivision of data by White's category of maternal diabetes will be done.

**Progress:** Data was collected on 16,893 births. The original PI (Dr. Beachy) left the Army and was to coordinate with Mr. Patience on the analysis of the data. No further work was done of the data analysis and this does not seem to be forthcoming so the protocol was terminated.

The principal investigator was changed from Dr. Joanna Beachy to Mr. Patience in Feb 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/013		<b>Status:</b> On-going
<b>Title:</b> The Role of Thrombospondin in Macrophage-Mediated Wound Healing. A Structural/Functional Dissection of Thrombospondin				
<b>Start Date:</b> 11/15/96		<b>Est. Completion Date:</b> Oct 98		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Aziz N. Qabar, MS				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Wound healing, thrombospondin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** To delineate the role of macrophage thrombospondin in the process of wound healing; to determine the mechanism(s) by which angiogenesis, associated with wound healing is controlled; and to analyze the functional and structural domain of thrombospondin.

**Technical Approach:** This study will examine the role of macrophages in wound healing. The profile of thrombospondin 1 and 3 secreted by activated macrophages will be tested in an in vitro system consisting of circulating monocytes (human monocytic cell lines, THP-1 and HL-60) which are activated with a phorbol ester or retinoic acid. Assays will consist of Western blots, metabolic labeling and immunoprecipitation, and Northern blots. The level of expression of each molecule will be determined quantitatively from developed autoradiographs. The level of regulation will be determined from the corresponding Northern blot, by comparing the profiles of the protein expression with that of its mRNA expression. A human TSP1/murine TSP3 chimera will be constructed using recombinant DNA techniques and PCR technology, resulting in a cDNA encoding the NH2-terminal of murine TSP3 and the COOH-terminal of human TSP1. A mutant form of the chimera will also be constructed, such that the two cysteine residues involved in S-S bridging in mTSP3 (Cys245 and Cys248) will be mutated into serine residues. The two chimeric proteins will be expressed in mammalian cells and their role on cell growth and differentiation will be investigated.

**Progress:** We found that activated macrophages also secrete another isoform of TSP1 name TSP3, that lacks the antiangiogenic domain of TSP1, with a distinct temporal pattern of expression. TSP3 failed to inhibit sprouting of vascular endothelial cells in vitro probably due to the absence of the anti-angiogenic domain of TSP1. Interestingly, we have found that three proangiogenic human breast cancer cell lines also overexpressed TSP1 and to a lesser degree proangiogenic TSP3. We probed the structure of each of the two molecules by creating a recombinant hybrid molecule and determined its effect on angiogenesis in vitro. Murine TSP3/Human TSP1 hybrid failed to inhibit angiogenesis in vitro although it contained 3/4 of human TSP1 molecule.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/118		<b>Status:</b> On-going
<b>Title:</b> Characterization, Tissue Expression, and Functional Studies of Alternate Splice Products of Human Steroidogenic Factor-1 (hSF-1)				
<b>Start Date:</b> 08/15/97		<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Meera S. Ramayya, M.D.				
<b>Associate Investigators:</b> George P. Chrousos, M.D.		COL Dan C. Moore, MC		
<b>Key Words:</b> human Steroidogenic Factor-1, transcripts, homologues, expression, cell culture system				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** 1) To determine the expression of hSF-1 in normal breast tissue, various types of human breast cancers, estrogen receptor (ER) negative breast cancer cells, ER positive native human breast cancer MCF-7 cells and MCF-7 cells treated with estradiol or tamoxifen using RT-PCR analysis; and 2) to determine the effect of transfection of hSF-1 on the growth of estrogen receptor positive and negative human breast cancer cells in the presence and absence of estradiol, tamoxifen or cAMP.

**Technical Approach:** Steroidogenic Factor -1 (SF-1), a tissue-specific orphan nuclear receptor, regulates the genes encoding several steroidogenic enzymes, Mullerian inhibiting substance, gonadotropins and StAR. In addition, SF-1 is crucial to hypothalamic, adrenal and gonadal organogenesis. StAR, a nonenzymatic protein, enhances the movement of cholesterol from the outer to the inner mitochondrial membrane. The human StAR (hStAR) has two hSF-1 response elements (SFRE's), which are essential for cAMP-dependent activation of the StAR gene. These response elements are identical to estrogen receptor response element (ERE) half sites. We will study the co-regulation of hStAR promoter-driven luciferase construct by hSF-1 and estrogen receptor  $\alpha$  (ER $\alpha$ ). We will perform co-transfection studies in HeLa cells to examine hSF-1's role as a regulator of the hStAR promoter through these SFREs. In addition we will examine the role of hSF-1 in the regulation of the ERE promoter of the oxytocin gene. We will study the co-regulation of oxytocin promoter-driven luciferase construct by hSF-1 and ER $\alpha$ . Finally we will perform gel-retardation studies with MCF-7 nuclear extracts to determine if ER derived from these breast cancer cells can bind to wild type and mutated SFRE's.

**Progress:** Dig labelled hSF-1 probes were made and expression of hSF-1 in MCF-7 cells was explored. Gel shift assays have been done to demonstrate binding of estrogen receptor to STAR gene promoter. Antibodies to hSF-1 will be tested for immunocytohistochemistry studies in the next phase of this study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/014		<b>Status:</b> Completed	
<b>Title:</b> Relationships Between A Female Soldier's Military Occupational Specialty (MOS) and Birth Outcomes					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> Jan 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b>					
CPT Robert J. Palowski, MS			Creedon FA		
MAJ Noble, MC			CPT Jennifer Aro, MC		
			Roxie Johnson, NP		
<b>Key Words:</b> Female soldiers:birth outcomes, MOS					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** The purpose of this investigation is to attempt to quantify risk utilizing Risk Ratio and Odds Ratio risk estimates and establish baseline rates for the offspring of female soldiers by Career Management Field (CMF) or MOS for the following outcomes: spontaneous abortions, ectopic pregnancies, intrauterine fetal demise, preterm birth, low birth weight infant, and as a mechanism to intervene in these adverse outcomes.

**Technical Approach:** A prospective cohort study will be performed at the following locations: Ft. Carson, Ft. Hood, Ft. Lewis, Ft. Bragg, Ft. Campbell, and Ft. Riley. Respondents will be enrolled during OB registration classes from 1 October 1994 through 31 January 1995 and then followed through September 1995 to allow the subjects to progress through their pregnancies and develop outcomes. All pregnant soldiers and pregnant wives and daughters of soldiers limited to those eligible for care. Demographic variables will be ascertained by way of a proctored questionnaire given to the mother at the time of the initial OB registration. Outcome data will be obtained through the use of a questionnaire located in the OB record, which will be compiled in the newborn nursery. The number of subjects required to provide sufficient power is estimated to be 5,000 composed of 1,670 soldiers and a comparison group of 3,330 spouses and daughters. The CMF/MOS's likely to meet these requirements are 91B and 92A. Soldier jobs could also be classified into the following categories for analysis: Medical Maintenance, Administrative, Logistics, Food Service, Law Enforcement, Communications, and Other.

**Progress:** 850 subjects were studied. All data have combined and data analysis is in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/139		<b>Status:</b> On-going	
<b>Title:</b> Pilot Study for Wound Healing Using Pulsed Electromagnetic Field Therapy					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> LTC John B. Whittemore, AN			MAJ Thomas K. Curry, MC		
<b>Key Words:</b> Pulsed Electromagnetic Field Therapy, wound healing					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** The overall objective is to determine whether pulsing electromagnetic fields (PEMFs) can potentiate post operative recovery by increasing the rate of incisional wound healing and decreasing pain management requirements in patients undergoing abdominal and vascular surgery whose wounds are left open for secondary closure. The objective of this particular study is to perform a pilot which will provide trained staff and practiced methodologies for a larger study.

**Technical Approach:** This project is designed as a pilot to test the objectives as described and to prepare personnel and methods for a larger study with more subjects. The study is designed as a semi-double blind, randomized, two-group experimental repeated measures design. Ten subjects will be randomly assigned to two groups of five each. One group will receive PEMF treatment and the other will receive placebo treatment. The study will be double-blinded for the PEMF technician as well as the evaluators. Subjects will be males or females, over 18 years of age, who have undergone abdominal or vascular surgery at MAMC and who have incisions healing by secondary intention. Patient information will be collected pertaining to pre-existing disorders that may act as confounding variables to normal wound healing. All eligible subjects will be sequentially entered into the study until the groups are full. Wound healing will be assessed by ASEPSIS (a wound healing and infection assessment), videothermography, photography, and plenography (a computer program used to trace and compare wound outlines). Post operative incisional pain will be assessed by a Visual Analog Scale and post-operative analgesic usage. Each variable will be initially analyzed separately. The non-parametric variables will be analyzed using a two-way, repeated measures, non-parametric analysis of variance. The parametric variables will be analyzed with a parametric repeated measures ANOVA.

**Progress:** This protocol never began due to lack of personnel. May get help in the next few months.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/153	<b>Status:</b> Terminated
<b>Title:</b> Use of Pulsing Electromagnetic Fields to Potentiate Healing of Stable, Open Ulcers on the Lower Limbs and Feet		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> Dec 97	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS		
<b>Associate Investigators:</b> MAJ Arnoldas S. Kungys, MC Melissa Wong, BA	LTC D. E. Casey Jones, MC Estelle Hamblen, BA, MHA	
<b>Key Words:</b> Pulsing electromagnetic fields, ulcers, feet, lower limbs		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To determine whether pulsing electromagnetic fields (PEMFs) can potentiate healing of stable, open ulcers on the lower limbs when used simultaneously with standard treatments relative to the rate of healing with placebo PEMF and standard treatment.

**Technical Approach:** Skin ulcers on the feet and legs are a highly significant clinical problem for patients with compromised neurovascular systems such as diabetics. We will perform a double blind study in which subjects will be randomly assigned to placebo PEMF and standard treatment or real PEMF and standard treatment. The patients will be those with diagnosed metabolic abnormalities (almost all will be diabetic) and have skin ulcers on their feet and lower legs which have not healed during the previous three months. Patients will be stratified by grade (I, II, III, and IV), location and diameter (< 1cm, 2.01 to 3.0 cm and >3.0 cm) of the ulcer as well as age and then randomly placed in either a placebo or real PEMF group. PEMF therapy (or placebo PEMF) therapy will be performed five days per week for one hour per day until the ulcer heals or six weeks. Rate of ulcer healing will be measured by photographing the ulcer on the first day of treatment and once every seven days for the duration of participation. A special high resolution, set distance, light controlled camera in conjunction with a planimeter to measure the cross-sectional area of the ulcer as recorded on the photographs will be used. Videothermograms will be taken nearly simultaneously with the light photographs from a standard distance using standard settings to evaluate changes in near-surface blood flow (very highly correlated with healing rate). A power analysis of previous results shows that 3 subjects will be needed in each group assuming (a) that we predict the PEMF group will do better (one-tailed test) and (b) an 80% chance of finding a difference between the two groups at a 0.05 level of significance. A total of about 80 subjects will be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

**Progress:** In previous years, the investigators performed an open trial with four diabetic patients with five open ulcers which had been stable in size for at least three months. Three healed entirely within three weeks with daily exposure to pulsing electromagnetic fields and the fourth healed in eight weeks. No further work was done on this study in FY 97 and it was terminated due to a lack of personnel.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/126		<b>Status:</b> On-going	
<b>Title:</b> Incidence and Impact of Headaches Among Users of Medical and Dental Facilities at Fort Lewis					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> MAJ Richard T. Dombroski, MC Steven A. Pace, MD 1LT Jan L. Sprauge, AN Melissa Wong, BA			MAJ Linda A. Marden, MC LTC Ann M. V. Bianchi, AN CDR Brian J. Kelly, MC Linda Robson, BA		
<b>Key Words:</b> Headache, Ft Lewis, WA, medical facility, dental facility					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** To determine the incidence and impact of headaches and low back pain among people eligible for care at military medical facilities. To estimate the utilization of medical facilities at Fort Lewis for treatment of headaches and low back pain. To estimate the cost of treating headaches and low back pain to the medical facilities at Fort Lewis.

**Technical Approach:** The proposed study had three parts: 1) distribute a two page survey of headache and low back pain activity and impact to a representative sample of people eligible for care at Ft. Lewis medical facilities. It will be distributed to people waiting in the Pharmacy, Pediatrics, Family Practice, Dental Clinics, Adult Primary Care Clinic, and the TMCs, as well as during annual physical exams in OB/GYN and Physical Exam. Additionally, it will be offered to over 2,000 ROTC Cadets in the summer. A power analysis of the response variability will be conducted after 1,000 responses and used to guide continued distribution. 2) Daily patient records from the ER, the TMCs, Family Practice and the Adult Primary Care Clinic will be prospectively reviewed for two months to identify patients with non-trauma headaches and their record will be reviewed for the history of treatment over the last two years. 3) A list of medications primarily prescribed for headaches will be compiled and the pharmacy will prepare (a) a record of how much of these prescriptions have been dispensed over the last two years and their costs and (b) a list of the people receiving these medicines. Every fifth name on a random sample of 500 people receiving those medications will be evaluated to insure that the medications are used for headaches.

**Progress:** 2,577 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/019		<b>Status:</b> On-going
<b>Title:</b> Treatment of Aura-Inaugurated Migraine Headache (Classic Migraine) with Pulsing Electromagnetic Fields: A Pilot Efficacy Study				
<b>Start Date:</b> 11/17/95		<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS				
<b>Associate Investigators:</b> Linda Robson, BA		MAJ Linda A. Marden, MC		
<b>Key Words:</b> Migraine, PEMF				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	11/15/96	

**Study Objective:** To determine whether classic migraine headaches can be treated with pulsing electromagnetic field (PEMF) therapy. This pilot will only determine whether the application of PEMF appears to have a clinically important effect. If it appears to have such an effect, larger, controlled studies will be proposed which will determine the extent and duration of the effect.

**Technical Approach:** We propose to have ten patients of either sex between the ages of 18 and 70 with at least a two year history of having classic migraines at least once per week keep a daily log of the frequency and intensity of headaches as well as medication use for two weeks. They will then be exposed to PEMF on the thigh at a power/frequency setting 6/600 for one hour per day, five days per week for three weeks. Analysis of headache activity will be performed by making a composite rating for each subject for each of the three rated periods (before, during, and after intervention). Activity for each period will be calculated for each variable by simply adding up the ratings (e.g. total hours of pain for the period) and by constructing a composite score equal to frequency times intensity for each period. The parametric measures (e.g. hours of pain) will be compared using a parametric, one way, repeated measures analysis of variance while non-parametric measures (e.g. pain intensity) will be evaluated using the non-parametric equivalent.

**Progress:** 17 subjects have been entered in FY 97, for a total of 30 subjects.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/085	<b>Status:</b> On-going
<b>Title:</b> Treatment of Headaches with Pulsing Electromagnetic Fields: A Multigroup, Double-Blind, Placebo-Controlled Study		
<b>Start Date:</b> 03/15/96	<b>Est. Completion Date:</b> Mar 97	
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS		
<b>Associate Investigators:</b> Linda Robson, BA LTC John B. Powell, MS		
MAJ Linda A. Marden, MC CPT Amy J. Asato, MC		
<b>Key Words:</b> Headache, PEMF, migraine, tension		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	03/21/97

Study Objective: To determine the duration and impact of pulsing electromagnetic field (PEMF) therapy on migraine and tension headache activity.

Technical Approach: We propose to have adult patients of either sex between the ages of 18 and 70 with at least a two year history of having headaches at least once per week keep a daily log of the frequency and intensity of headaches as well as medication use for two weeks. They will be stratified by type of headache (either migraine with aura, migraine without aura, migraine associated with the menstrual cycle, tension headache, and mixed migraine - tension headache) and randomized into actual or placebo PEMF therapy. They will then be exposed to PEMF (real or placebo) on the thigh at a power/frequency setting of 6/600 for one hour per day, five days per week for two weeks. Neither the therapist nor the patient will know which group they are in. A two week stabilization period will follow the two weeks of real or placebo therapy. Patients will keep a headache log during this period. The next stage will cross-over the subjects. At the end of this period, patients will keep a two week follow-up log and be followed-up by phone at one month, three months, and six months after the end of therapy. Patients will be instructed to call us when their headaches have returned to pre-treatment levels. Standard treatment will be offered at that time. Success is usually defined as at least a 50% decrease in headache activity as calculated from a composite score based on frequency, duration, and intensity with a commensurate decrease in medication use. We will perform a power analysis after the first five patients complete the post-treatment log to determine the number which will probably be required. We will request permission to increase our number of subjects if more than a total of 100 subjects are required to differentiate between groups if the differences are such that differentiating between groups would be worthwhile.

Progress: 45 subjects have been entered in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/151		<b>Status:</b> Completed
<b>Title:</b> Short-term Stability and Habituation of Human Finger Blood-Flow				
<b>Start Date:</b> 09/20/96		<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS				
<b>Associate Investigators:</b> Melissa Wong, BA		Linda Robson, BA		
<b>Key Words:</b> Blood flow:finger				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** To determine the short term stability (half an hour) of human finger blood flow and any habituation which may occur to the recording environment over the course of three recording sessions. This is necessary in order to determine how long patients need to sit quietly after being instrumented for finger temperature recordings before stabilization occurs and interventions can begin. Changes in length of time required for stabilization across sessions as habituation occurs also needs to be determined so the amount of time required can be anticipated and planned for in multi-session treatments and studies.

**Technical Approach:** Ten subjects who are healthy employees of Madigan AMC will walk from their places of work to the test room in Orthopedic Clinic and be seated upright in a comfortable recliner. A thermistor probe will immediately be taped to the left edge of the left index finger just above the distal joint and temperatures will be documented every thirty seconds for one half hour. The hand with the probe attached will be kept relatively still on the padded arm of the chair for the entire recording period. A videothermograph will be focused on the hand to produce continuous recordings of near surface blood flow in the hand. Participants will be asked to minimize movement and talking while being encouraged to sit quietly and relax with eyes open or closed as they wish. Each subject will participate in three of these half hour sessions at the same time of day once per week for three weeks. Pilot data show that ten subjects should be sufficient to establish the amount of variability which can be expected. Recordings made by the thermistor and the videothermograph will be correlated. Confidence intervals for variability will be established and the data will be displayed in both tabular and chart form so clinicians and investigators can use their own stabilization criteria to establish an optimal stabilization period for their own needs.

**Progress:** Twenty-six subjects were entered. This study illustrates the importance of permitting stabilization to occur prior to recording fingertip temperature for psychophysiological applications. Three protocols were performed to illustrate different problems. In the first, fingertip temperatures of three experienced biofeedback providers and three staff naive to biofeedback were recorded for five minutes after they entered a typical biofeedback room. The three experienced subjects showed minimal change from baseline (+0.3, -0.2, +0.1) while the three naive subjects showed increases of 2.3, 7.7, and 11.0 degrees. In the second protocol, ten biofeedback naive subjects were recorded as above for ten minutes. They required up to seven minutes for the temporary initial stabilization to occur. There was a strong negative correlation between amount of change in temperature and initial fingertip temperature. In the third protocol, ten additional biofeedback naive subjects were recorded as above for 30 minutes in three half hour sessions spaced a week apart. Few of the patients showed decreased variability across sessions. Several subjects showed increases or decreases in temperature for the entire half hour session.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/109		<b>Status:</b> Terminated	
<b>Title:</b> Biofeedback Measures of Pelvic Floor Muscle Function in Incontinent and Asymptomatic Women					
<b>Start Date:</b> 06/20/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b>			Tries JM		
<b>Key Words:</b> Urinary incontinence, biofeedback					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To answer four questions: a) to what degree do measures of pelvic floor function differ between incontinent and "optimum" asymptomatic women; b) to what degree do EMG measures of pelvic floor function change as a result of a single biofeedback training session which is designed to decrease extraneous abdominal muscle activity that might occur during a 10-second contraction of the pelvic floor muscles; c) to what degree is the surface measure of abdominal EMG a valid index of intra-abdominal pressure as measured by a rectal balloon; and d) to what degree are surface measures of EMG in the proximal and distal regions of the anal canal valid indices of pressure as measured in the same regions of the canal, respectively.

**Technical Approach:** 1) Two groups will be studied, one with urinary incontinent women, the other group, to be run at MAMC, will be composed of female soldiers in excellent physical shape who are asymptomatic, nulliparous which will serve as "optimum" control. It is very difficult to find a large group of healthy women in excellent physical shape but who are not "professional" athletes in the civilian community so the military population seems ideal for finding out what optimum values are likely to be. 2) Both groups will be interviewed before data collection process but it is anticipated that the asymptotic interview will be only 10 minutes compared to the 30 minutes required of the incontinent subjects. Informed consent could be obtained at this time. Exclusion criteria include: allergy to latex or adhesives typically used on the body; a history of neurologic, metabolic inflammatory, or congenital bowel or bladder disorder; benign ano-rectal defects; psychiatric illness; frequent bladder infection greater than one in past 3 years; gynecologic or pelvic injury; chronic constipation or straining with stool; urinary or fecal urgency; and urinary or fecal incontinence after the age of eight. 3) Both groups will undergo an initial EMG measurement procedure. They will be asked to rest, contract and push out the anal canal recording probe. This will take about 15 minutes. 4) Both groups will be then trained to produce a more isolated pelvic floor contraction using an abdominal threshold to reinforce inhibition of extraneous abdominal contraction during PFM contraction by at least 50% of that recorded during the initial EMG assessment. All subjects will have 26 contraction trials with feedback. Each trial will take a maximum of 10 seconds with a 10-20 second rest period between each contraction. 5) After the training and a 10 minute rest, the EMG assessment will be repeated but subjects will receive feedback during the assessment. 6) After the EMG assessment, pressure measures will be obtained using the Schuster balloon. The asymptomatic subjects will be debriefed and discharged, the incontinent subjects will be given a home program and scheduled for subsequent treatment.

**Progress:** This study was terminated because a sufficient number of subjects could not be obtained.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/131		<b>Status:</b> Completed	
<b>Title:</b> Treatment of Inflammation Related Low Back Pain with Pulsing Electromagnetic Fields: A Pilot Efficacy Study					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> May 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> CPT Marc J. Michaud, MC			LTCR Clayton E. Turner, MC		
<b>Key Words:</b> Low back pain, PEMF, inflammation					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine whether inflammation related to low back pain can be treated with pulsing electromagnetic field (PEMF) therapy. This pilot will only determine whether the application of PEMF appears to have a clinically important effect. If it appears to have such an effect, larger, controlled studies will be proposed which will determine the extent and duration of the effect.

**Technical Approach:** We propose to have ten adult patients of either sex between the ages of 18 and 70 with at least a two year history of having chronic, daily musculoskeletal low back pain with symptoms of inflammation keep a daily log of the frequency and intensity of back pain as well as medication use for two weeks. They will then be exposed to PEMF over the lower back at a power/frequency setting of 6/600 for one hour per day, five days per week for two weeks. This should be more than sufficient time to produce an effect. They will continue keeping the pain log during and for two weeks after the PEMF exposure. The trial will be considered successful if half of the patients report any combination of at least a fifty percent decrease in pain with no change in medication or a twenty-five percent decrease in pain with reduced use of pain medications. Patients will have a videothermographic evaluation of their lower backs before and after treatment to assess changes in inflammation. Analysis of changes in back pain will be performed by comparing each subject's pain during each of the three rated periods. Parametric measures (length of pain) will be compared will be measured using parametric one-way, repeated measures analysis of variance while the non-parametric measures (pain intensity) will be evaluated using the nonparametric equivalent. Changes in temperature patterns of the low back will be evaluated using a paired t-test of changes in the difference in absolute temperature between the left and right sides of a three cm square area centered over the bulk of the paraspinal muscles at L4 IAW Psychophysiology Laboratory SOPs.

**Progress:** Ten patients were exposed to pulsing electromagnetic fields. Minor improvements for five of the subjects disappeared at the end of the two-week exposure period. The study was terminated because the intervention was ineffective.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/058		<b>Status:</b> On-going	
<b>Title:</b> Determination of whether a Pronation-Controlling Insole Reduces the Occurrence of Lower Limb Pain Among Overpronating Soldiers During Basic Training					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS					
<b>Associate Investigators:</b> L. Crane			L. M. Vonasek		
<b>Key Words:</b> Pronation, insole, lower limb pain					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine whether a pronation-controlling insole reduces the occurrence or extent of overpronation-related lower limb pain and injuries among overpronating U.S. Army recruits in basic training compared with similar overpronating trainees who do not use the insoles. Because pain and some minor injuries may not be reported, we will measure parameters such as PT test scores which are likely to be effected by these problems. We will also factor out reports of pre training lower limb pain and injuries as well as changes in exercise.

**Technical Approach:** During basic training the enrolled trainees will be monitored for 1) raw-physical fitness test scores, 2) number of trainees graduating on time, 3) number of visits to the clinic for lower limb pain, 4) number and severity of lower limb injuries. The physical fitness test, which consists of a timed 2-mile run and timed push-ups and sit-ups, is given for record at the beginning and at the end of basic training. For purposes of this protocol, minor lower limb pain injuries are rated as 1) pain with no change in activities, 2) pain with decreased activities 3) pain with rest. After four weeks of training, the inserts will be replaced with new ones and the used ones will be returned to the sponsor for evaluation. This is necessary so trainees will not be using worn inserts. Subjects will rate their pain on a colored visual analog scale that shows a continuous gradation of colors from white, indicating no pain, to bright red, indicating the maximum pain. The continuous scale is marked with 0 through 10 with zero indicating no pain and 10 indicating maximal pain. At the completion of this basic training the enrollees will complete a questionnaire that asks about overall frequency of use of inserts, use during physical training, use during road marches, use during class time, lower limb pain during basic training, and injuries during training. This information was successfully gathered from this population at the proposed test site without significant problem.

**Progress:** 361 subjects have been entered in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/158		<b>Status:</b> On-going
<b>Title:</b> Pilot Study For: Environmental-Temporal Relationships Between Changes in (a) Paraspinal Muscle Tension and Low Back Pain and (b) Trapezius Muscle Tension and Migraine and Tension Headache Intensity				
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Feb 97	
<b>Department:</b> Clinical Investigation			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Richard A. Sherman, MS				
<b>Associate Investigators:</b>			Melissa Wong, BA	
Christie Hill			Linda Robson, BA	
Estelle Hamblen, BA, MHA			Kimberly A. Hermann-Do, BS, MHA	
Antje F. W. Goeken, Psy.D.				
<b>Key Words:</b> Muscle tension:paraspinal, Muscle tension:trapezius, migraine, low back pain				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** 1) To determine whether there is a temporal relationship between changes in paraspinal muscle tension and changes in musculoskeletal low back pain in patients' normal environments. 2) To determine whether there is a temporal relationship between changes in trapezius muscle tension and changes in intensity of migraine and tension headaches in patients' normal environments. 3) To determine whether environmental - temporal relationships between (a) musculoskeletal low back pain and paraspinal muscle tension pain and (b) trapezius muscle tension and migraine and tension headache change after successful biofeedback therapy.

**Technical Approach:** There will be ten subjects in each group with the groups consisting of patients diagnosed as having tension headaches, musculoskeletal low back pain, migraine headaches, or mixed migraine-tension headaches (a total of 40 patients). Ten subjects per group are likely to be needed to detect consistent temporal relationships between pain and muscle tension reliably because the previous data were highly variable and idiosyncratic. Assignment to groups will be by diagnosis only as there are no controls, etc. The subjects will all be patients referred from the TMC's at Ft. Lewis or the Neurology and Family Practice clinics at Madigan AMC who meet the diagnostic criteria for entrance into the study. They will be between 18 and 55 years of age, be otherwise healthy, and of either sex. Each subject will have four consecutive days of ambulatory recordings during all waking hours before and after standard muscle tension awareness and control treatment which will take approximately six weeks. Headache patients will have their bilateral trapezius muscled tension recorded while low back pain patients will have their paraspinal muscles recorded. The motion sensor will be placed in the center of the back between the shoulder blades for all patients. The recorded will beep every hour to remind the subjects to record their pain levels and type of activity being engaged in. the beeper does not stop until a pain rating is entered on the keyboard. The intervention/treatment is not experimental and will be performed (and its success rated) according the Surgical Research Service SOPs.

**Progress:** 18 subjects have been entered in FY 97, for a total of 39 subjects.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF DENTISTRY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/053		<b>Status:</b> On-going	
<b>Title:</b> A Survey of Sedation and General Anesthesia Techniques of the Oral and Maxillofacial Surgery Practitioner					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Dentistry			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ David K. Fiaschetti, DE					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Srugery:maxillofacial, anesthesia, sedation					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

Study Objective: 1) Establish current trends in sedation and general anesthesia techniques used by practitioners in Oral and Maxillofacial Surgery. 2) To determine pharmacological agents used and methods of administration of these agents. 3) Determine availability and usage of monitoring and emergency equipment.

Technical Approach: A national survey of members of the American Association of Oral and Maxillofacial Surgeons will be conducted to update information on sedation and general anesthesia techniques used by Oral and Maxillofacial Surgeons. A statistical set number of randomly selected members will be mailed questionnaires. Practitioners will be questioned concerning their anesthetic techniques to include anesthetic drugs used, methods of delivery, composition of the anesthesia team, as well as anesthesia, monitoring and emergency equipment available. Demographic data will be collected on years in practice, solo vs. group practice, location and practitioner's training. Establishment of current patterns and trends will be made.

Progress: 1,350 surveys have been mailed. Response rate has been 48% to date. Debating whether to send out a second mailing.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/046		<b>Status:</b> On-going	
<b>Title:</b> Evaluation of the Efficacy of Post-operative Antibiotics After Orthognathic Surgery					
<b>Start Date:</b> 01/19/96			<b>Est. Completion Date:</b> Nov 96		
<b>Department:</b> Dentistry			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Henry W. Marcantoni, DE					
<b>Associate Investigators:</b> COL Andrew A. Vorono, DE MAJ Thomas J. Borris, DE			LTC Charles R. Weber, DC MAJ Timothy Bandrowsky, DE		
<b>Key Words:</b> Surgery:orthognathic, penicillin G, penicillin VK, cefaxolin, cephradine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					09/19/97

**Study Objective:** To compare the efficacy of a standard perioperative antibiotic regiment with and without a one week postoperative antibiotic regimen for patients undergoing orthognathic surgery in a prospective, randomized, double-blind study.

**Technical Approach:** Either isolated mandibular bilateral sagittal split ramus osteotomies, isolated maxillary Lefort I osteotomies, or a combination of the two procedures will be performed on all patients enrolled in the study. Patients in each operative group will be further subdivided randomly into one of two groups. The experimental group will receive prophylactic antibiotics as follows: one preoperative dose and intraoperative doses at two hour intervals for the duration of the surgery. The control group will receive the same preoperative and perioperative regimen along with a seven day oral postoperative regimen. The patients will be monitored for objective signs of infection, and WBC counts will be drawn preoperatively and post-operatively at one week.

**Progress:** 8 subjects were entered during FY 97, for a total of 40 subjects.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF  
EMERGENCY MEDICINE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/014		<b>Status:</b> Terminated	
<b>Title:</b> Patients Who Leave A Military Hospital Emergency Department Without Being Seen by a Physician					
<b>Start Date:</b> 11/17/95			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard D. Brantner, MC					
<b>Associate Investigators:</b>			CPT Constance A. Lavieri-Reynolds, MC		
<b>Key Words:</b> Emergency treatment, patient not seen by a physician, outcome					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** (1) To develop identifiers that may aid in early recognition of patients who leave the emergency department without being seen. (2) To compare the medical outcomes of patients who leave without being seen to determine if they are at risk for poorer outcomes than patients who stay to be seen by a physician.

**Technical Approach:** This study will involve all patients who register for care in the MAMC Department of Emergency Medicine who leave prior to being seen by a physician. The sample size is estimated to be approximately 500-600 patients over the course of 6 months. The patients will be identified through the QA/QI system already established and begins when the triage nurse call the patient's name three times without a response. In this system, the chart is reviewed, an attempt is made to contact the patient, and the patient is then discharged out of the computer system. Under this protocol, patients who leave without being seen will receive additional attempts to contact by phone or mail for 3 days following their ER check-in. Charts will be collected and reviewed for particular characteristics which will be recorded. Patients contacted within the three days will be asked to answer a questionnaire which includes questions on their demographics, reason for leaving the ER, length of wait before leaving, further treatment sought and current status. Questionnaires will be given either telephonically or by mail. These will be compared to patients who went through with an ER visit and answered the same questionnaire. The characteristics and medical outcomes of the two groups will be compared using the student's t-test, chi-square and regression analysis for statistical significance.

**Progress:** This protocol has been terminated. The initial PI (CPT Constance A. Lavieri Reynolds, MC) was transferred before work could be started on the protocol. The protocol was transferred to Dr. Brantner who was unable to perform the protocol due to time constraints.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 93/120		<b>Status:</b> Terminated	
<b>Title:</b> The Randomized Use of Helium-Oxygen Mixture for the Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease. A Blinded Trial					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Dec 93		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard D. Brantner, MC					
<b>Associate Investigators:</b> CPT David A. Della-Giustina, MC MAJ Bernard J. Roth, MC			CPT James W. Thompson, MC MAJ Timothy R. Murray, MC		
<b>Key Words:</b> COPD, helium,oxygen					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$800.00
					<b>Periodic Review:</b> 04/21/95

**Study Objective:** To determine the therapeutic role of Heliox administration in the treatment of acute exacerbation of chronic obstructive pulmonary disease.

**Technical Approach:** Patients presenting with an acute exacerbation of COPD and requiring urgent treatment and agree to participate will be randomized to receive either Heliox (a mixture of 75% helium and 25% oxygen) or nitrogen-oxygen (a mixture of 75% nitrogen and 25% oxygen). Pulse oximetry will be monitored and any patient whose level falls to less than 90% will receive supplemental oxygen at a rate sufficient to raise pulse oximetry to at least 90%. Spirometry will be performed to measure FEV<sub>1</sub>, FVC, and PEF. Base line arterial blood gas analysis will be performed and an upright portable chest x-ray will be obtained. Patients will be asked to score the severity of symptoms and the time to relief of those symptoms. All patients will receive nebulized albuterol treatments every thirty minutes for a total of 3 treatments. Patients will be re-evaluated after each treatment and at the end of the 90 minutes study period all patients will be placed on room air. Ten minutes after discontinuation of heliox or nitrogen-oxygen treatment, an arterial blood gas will be obtained, spirometry performed and the patients will be instructed not to discuss or divulge the mode of treatment they received. Patients will be evaluated at this time by a pulmonologist who will be blinded as to the treatment used. After evaluation of the patient, baseline and end of study data a determination will be made for 1) probable admission, 2) possible admission, 3) or admission not necessary.

Biographical data will be evaluated using the t-test. The subjective rate of improvement in symptoms between the groups will be analyzed using the Mann-Whitney U Test and percentage improvement in FEV<sub>1</sub> will be compared using regression analysis.

**Progress:** One new patient was enrolled in this study in FY 97. The study was terminated due to equipment failure that was necessary for subject evaluation plus the reassignment of the principal investigator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/116		<b>Status:</b> Completed	
<b>Title:</b> Multicenter, Prospective, Double-Blind Randomized Comparative Trial to Evaluate the Treatment Effects of Ciprofloxacin for 7 Days, Compared with Standard Therapy for 14 Days, In...acute Pyelonephritis					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Thomas F. Burke, MC					
<b>Associate Investigators:</b>			COL Ronald H. Cooper, MC		
COL Eugene T. Etzkorn, MC			LTC Joseph T. Morris III, MC		
Carlos Falcon, M.D.			MAJ Darrell E. Griffin III, MS		
David E. Bell			MAJ William T. Hurley, MC		
<b>Key Words:</b> pyelonephritis, ciprofloxacin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		06/21/96	

**Study Objective:** To compare the treatment effects of ciprofloxacin (IV single dose/PO or PO) versus standard therapy (IV single dose/PO or PO) as outpatient management in premenopausal females with acute uncomplicated pyelonephritis. The efficacy and tolerability of a seven day treatment of ciprofloxacin will be compared with a fourteen day treatment with standard therapy. In addition, healthcare resource utilization will be evaluated related to treatment drop-outs, failures/relapses, as well as adverse events between both treatment arms (direct costs). Patient perception will be collected by recording patient's speed of recovery and return to normal activity.

**Technical Approach:** Premenopausal women with clinical signs and symptoms of acute pyelonephritis and pyuria are eligible to participate in this study. After enrollment, study drug (ciprofloxacin or Trimethoprim/Sulfamethoxazole) may be administered as an initial single IV. dose, or oral dose, followed by oral therapy for a total duration of therapy of 14 days of active study medication for the control arm, versus 7 days of active drug for the investigational arm, followed by 7 days of placebo. All patients enrolled in the trial (including failures and drop-outs) will be followed until 4-6 weeks following the completion of study drug. The primary outcome parameter will be bacteriological and clinical efficacy. A secondary parameter is the overall costs associated with pyelonephritis treatment of the two regimens. Patient perceptions will be collected by questioning the patient regarding their response to treatment.

**Progress:** This multicenter study was closed to enrollment by the sponsor in Dec 96. Sixty-three patients were randomized to study drug; 17 patients were dropped for various reasons such as no causative organisms found, inability to swallow study medication, and adverse events that were not considered to be related to the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/055		<b>Status:</b> On-going	
<b>Title:</b> A Randomized, Double-Blind, Multicenter Trial Comparing 10 Days of Oral Therapy with Trovafloxacin - CP-99,219 and 14 days of Oral Clarithromycin for the Treatment of Acute Sinusitis					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Apr 98		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John D. Charette, MC					
<b>Associate Investigators:</b> CPT Janice C. Stracener, MC			Steven A. Pace, MD CPT Daniel Mcilmail, MC		
<b>Key Words:</b> Sinusitis, Trovafloxacin, Clarithromycin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

**Study Objective:** To compare the safety and efficacy of Trovafloxacin (CP-99,219) and Clarithromycin in the treatment of subjects with acute sinusitis.

**Technical Approach:** A total of 250 ambulatory subjects, aged 18 or more with a medical history and clinical and radiological findings consistent with acute sinusitis will be included. Subjects with acute sinusitis will be randomized in a double-blind fashion to receive either Trovafloxacin 200 mg once daily for 10 days or Clarithromycin 500 mg twice daily for 14 days.

All subjects enrolled will be evaluated at baseline for clinical signs and symptoms of acute sinusitis, including purulent sinus discharge, facial pain, headache, hyposmia, nasal congestion and jaw pain on mastication. In addition, subjects must have findings of acute sinusitis on sinus X-ray. Sinus puncture for microbiological diagnosis is desirable but not required.

Clinical response to therapy will be assessed by the investigator at day 4, end of therapy (day 15), and end of study (day 28). The clinical response will be based primarily on the global assessment of the clinical presentation of the subject at the evaluation timepoint but compared to the pretreatment assessment. It will be strongly recommended that subjects who fail to respond to treatment should undergo trans-antral aspiration of the sinus for microbiological assessment.

Routine laboratory safety tests will be undertaken pre treatment, at day 4, and end of therapy (day 15). They will be repeated at day 28 if an abnormal result is detected at the end of therapy visit.

**Progress:** 8 subjects were consented, with 6 actually receiving study medication.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/116		<b>Status:</b> On-going	
<b>Title:</b> Incidence of Intravenous Prochlorperazine-Induced Akathisia					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Daniel L. Drotts, MC					
<b>Associate Investigators:</b> CPT David R. Vinson, MC			CPT Richard D. Brantner, MC		
<b>Key Words:</b> Akathisia, prochlorperazine, migraine, antiemetic					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To determine the incidence of IV prochlorperazine-induced akathisia.

**Technical Approach:** Akathisia, the syndrome of motor restlessness, is an intensely unpleasant, fairly common side effect of prochlor-perazine. This study will investigate the incidence of akathisia in Emergency Department patients who receive intravenous prochlorperazine as per usual standard of care. The study patient (any ED patient for whom prochlorperazine alone is indicated) will receive IV prochlorperazine as per published PDR guidelines. Occurrence of akathisia will be determined by a previously validated akathisia scale at time 0, 30 minutes. We intend to use this incidence data in a follow on study using the same akathisia tool and study setting. This second, prospective, double-blinded, placebo-controlled study, will be designed to determine the efficacy of diphenhydramine in preventing prochlorperazine-induced akathisia.

**Progress:** 100 subjects were enrolled in FY 97, for a total of 140 subjects. Two abstracts have been submitted.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/062		<b>Status:</b> Completed	
<b>Title:</b> Out-of-Hospital Initiated Intravenous Lines: Are We Starting Too Many?					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Fritz Fuller, N.R.E.M.T.-P					
<b>Associate Investigators:</b> T. Dahlgren			CPT Robert H. Lutz, MC		
<b>Key Words:</b> IV lines:out of hospital					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine the incidence, cost and the causative characteristics of overutilized out-of-hospital IV's.

**Technical Approach:** Paramedics operating under standing orders (protocols) have enormous latitude in deciding which patients require and receive intravenous (IV) catheter placement. Numerous factors enter into this decision making process including, distance to the receiving center, perceived severity, provider experience level, and the presence of paramedic students. A pilot study conducted by the Pierce County Quality Improvement Committee showed an overutilization rate equal to 26% (31/120). These EMS patients had a field IV started that was never utilized for fluids and/or medications in either the field or during the emergency department stay. The simple act of starting these IV's increases charges, creates occupational hazards, and inflicts pain upon the patient. We proposed to prospectively gather data on patients delivered to two area hospitals (one community and one teaching hospital) by Shepard Paramedics to determine how often IV's are being initiated by paramedics without medical control and then never utilized.

**Progress:** 290 patients were included during a 34-day study period; 165 had an IV initiated (147) or attempted (18). Twenty-nine percent of the patients received an unnecessary (over-treatment) IV. 125 patients did not have an IV initiated and seven subsequently required IV fluid bolus or medications within the first 60 minutes. The unnecessary IV placement rate of 20% was much larger than initially hypothesized (10%). Only the presence of a paramedic student slightly increased the odds (2.4) of unnecessary IV placement ( $p < 0.05$ ). The under-treatment rate was 2.4%.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/020		<b>Status:</b> On-going
<b>Title:</b> A Model for Prehospital 12-Lead Acquisition Without A Dedicated 12-Lead ECG Machine				
<b>Start Date:</b> 02/21/97		<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Fritz Fuller, N.R.E.M.T.-P				
<b>Associate Investigators:</b> LTC Alice M. Mascette, MC		Steven A. Pace, MD		
<b>Key Words:</b> ECG:12 lead				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** To verify that a 12-lead ECG obtained with a cardiac monitor/defibrillation unit is comparable in accuracy to that of a dedicated 12-lead ECG machine.

**Technical Approach:** The management of ischemic chest pain and acute myocardial infarction hinges on early diagnosis and treatment with thrombolytic agents if indicated. It has been shown that prehospital recognition of acute MI using 12-lead electrocardiography and interpreted by nurses/paramedics trained in ECG evaluation can result in significantly faster times to thrombolytics compared to patients who did not receive a prehospital ECG. Today there are several portable 12-lead machines with computer assisted diagnosis available, but they have only recently become available and are very expensive. By utilizing a portable 12-lead machine (Lifepak 10) and demonstrating that it can produce diagnostic quality ECG's, we hope to make available to a large group of prehospital providers 12-lead capability without an increased monetary investment.

**Progress:** 50 subjects (100 tracings) have been entered. One physician has reviewed all the tracings, the other is still in the process of reviewing them.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/189		<b>Status:</b> Completed	
<b>Title:</b> Analgesia for Reduction of Acute Glenohumeral Dislocation: Intra-articular Lidocaine Versus Intravenous Fentanyl					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Aug 96		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Joseph R. Hoffman, MC					
<b>Associate Investigators:</b> MAJ Marco Coppola, MC			CPT Richard Butler, MC CPT David A. Siegel, MC		
<b>Key Words:</b> Glenohumeral dislocation, lidocaine, Fentanyl					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

Study Objective: We intend to contrast the analgesic efficacy of intra-articular lidocaine versus intravenous fentanyl in an adult population suffering from acute glenohumeral dislocation.

Technical Approach: A sample of 40 consenting patients (male and female) meeting diagnostic and inclusion criteria would be enrolled in the study. They would be randomized to receive either intravenous fentanyl or intra-articular lidocaine as analgesia for the reduction of their shoulder dislocation. Reduction would be performed by a standardized technique and their shoulder immobilized for post-reduction radiographs. Patients would be asked to rate their pain at presentation, pain at the administration of analgesia, pain of reduction, level of sedation, and pain at time of discharge on a visual analog scale. The clinician would also rate the ease of reduction. Data would undergo analysis of variance (ANOVA). The patient's score and the physician's score would be subjected to regression correlation.

Progress: The combined data from MAMC & Darnell Army Hospital is being analyzed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/028		<b>Status:</b> On-going
<b>Title:</b> Prospective, Randomized, Double-Blind Comparison of the Safety and Efficacy of BAY 12-8039 400 MG QD x 10 Days vs 400 mg QD x 5 Days vs Clarithromycin 500 mg BID x 10 Days for the Treatment of ...				
<b>Start Date:</b> 11/15/96		<b>Est. Completion Date:</b> Jan 98		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Bronchitis, BAY 12-8039, clarithromycin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		11/21/97

**Study Objective:** To compare the safety and efficacy of BAY 12-8039 QD x 5 days vs BAY 12-8039 400 mg QD x 10 days vs clarithromycin 500 mg BID x 10 days for the treatment of acute bacterial exacerbations of chronic bronchitis. The study will include comparisons of the clinical and bacteriological responses of the three regimens during, at the end of therapy and at the follow-up time points. The safety of the three treatment regimens will also be compared.

**Technical Approach:** This is a prospective, randomized, double-blind, multicenter study comparing the safety and efficacy of BAY 12-0839 400 mg QD x 5 days vs. BAY 12-0839 400 mg QD x 10 days vs clarithromycin 500 mg BID x 10 days for the treatment of patients with acute exacerbations of chronic bronchitis. The duration of therapy will be 10 days of study drug with a 21-28 day follow-up period. Patients will be seen on day 3-5 of treatment, 2-4 days after treatment, 7-14 days after tx and 21-28 days after tx. A sputum culture will be obtained at each visit, and CBC and chemistries will be monitored periodically for abnormalities.

**Progress:** 3 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/062		<b>Status:</b> Completed	
<b>Title:</b> Double-Blind, Randomized, Comparative, Multicenter Study of Zagam (Sparfloxacin) vs. Biaxin (Clarithromycin) in the Treatment of Community-Acquired Pneumonia					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b> D. W. Schroeder			MAJ Thomas F. Burke, MC J. Halper		
<b>Key Words:</b> Pneumonia, sparfloxacin, clarithromycin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To evaluate the efficacy and safety of sparfloxacin (RP 65206) compared with clarithromycin when administered orally for 10 consecutive days in the treatment of patients with community acquired pneumonia.

**Technical Approach:** This is a double-blind, randomized, double-dummy, comparative, multicenter study of sparfloxacin versus clarithromycin in the treatment of patients with community-acquired pneumonia. A total of 380 patients will be recruited from 30 participating sites. After meeting the inclusion/exclusion criteria and giving informed consent, patients will be randomly assigned to receive either a loading dose of 400 mg sparfloxacin (two 200 mg tablets) followed by sparfloxacin 200 mg (one 200 mg tablet) QD, or clarithromycin 500 mg q 12h, each for 10 days. A double-dummy system will be used such that matching comparator placebos will be given concurrently with the active drug during the treatment period. Patients will be required to visit the study site at baseline, on day 4 during treatment, on day 20 (10 days after treatment) and for long-term follow-up on day 38 (28 days after treatment). Efficacy will be assessed as the clinical response. Safety of sparfloxacin and clarithromycin will be assessed using subjective patient reports, clinical evaluations and laboratory tests.

**Progress:** Three patients completed this study. One adverse event, not related to the study medication, was reported at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/152		<b>Status:</b> Terminated	
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret Model					
<b>Start Date:</b> 08/16/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b>			MAJ Thomas F. Burke, MC		
MAJ Lawrence A. Wilson, MC			MAJ Mary P. Fairchok, MC		
COL Patrick C. Kelly, MC			COL Robert V. Jarrett, MC		
MAJ Thomas D. Carver, MC			MAJ Roger M. Hinson, MC		
<b>Key Words:</b> Intubation:training, animal model, ferret,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					06/21/96

Study Objective: To enhance the clinical skills of health care providers in managing pediatric airways, specifically endotracheal intubation.

Technical Approach: Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube. Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure.

Progress: Two training sessions were held in FY 97, utilizing a total of 7 animals. This protocol was terminated in Aug 97, due to the three year approval limit.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/165		<b>Status:</b> Terminated	
<b>Title:</b> Emergency Surgical Procedures Laboratory Training Utilizing the Goat (Capra hircus)					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b> MAJ Lawrence A. Wilson, MC			MAJ William J. Frohna, MC		
<b>Key Words:</b> Emergency surgical procedrues: training, goat,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		01/19/96	

Study Objective: The objectives of this training exercise are to teach physicians one safe method of performing six life-saving procedures for trauma patients.

Technical Approach: The procedures listed below will be performed under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures. The procedures consist of: 1) Chest tube insertion, 2) Cricothyroidotomy, 3) Pericardiocentesis, 4) Diagnostic peritoneal lavage, 5) Venous cutdown, 6) Thoracotomy.

Progress: Two sessions were held in FY 97, utilizing a total of 8 animals. The protocol was terminated in Sep 97 due to the expiration of the three year approval period. A new protocol is being rewritten to replace this training protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/133		<b>Status:</b> On-going	
<b>Title:</b> Pain Treatment and Documentation by Paramedics					
<b>Start Date:</b> 10/17/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b>			Fritz Fuller, N.R.E.M.T.-P		
<b>Key Words:</b> Pain, morphine, out-of-hospital documentation, pramedics					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To determine the frequency of out-of-hospital documentation of pain and morphine administration to trauma patients who are in pain. Subgroups including burns and long bone fractures will be identified and frequency of morphine use in these groups will also be determined. Other variables such as age, gender, documentation of the presence of pain, mental awareness and recent drug or alcohol use will be analyzed to determine their associations with morphine use.

**Technical Approach:** Patients will be identified by a manual search of all patient care records from Shepard Paramedics for the 6 month study period. Records meeting inclusion criteria will then be copied and attached to a standardized data collection form. Someone blinded to the purpose of the study will then abstract the relevant data from these sheets. One of the authors will then pull the data from the abstraction sheets and enter it into a computerized data base for analysis.

**Progress:** New protocol that has not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/139		<b>Status:</b> On-going	
<b>Title:</b> A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter Study to Investigate the Efficacy and Safety of Inhaled Zanamivir (GG167) 10 mg Administered Twice a Day for Five Days.....					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Apr 98		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Steven A. Pace, MD					
<b>Associate Investigators:</b> CPT Mark Buettner, MC			CPT Michael A. Miller, MC		
<b>Key Words:</b> Influenza, zanamivir, efficacy, safety, tolerability					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** 1) To evaluate the efficacy of inhaled zanamivir compared to placebo in the treatment of influenza A and B viral infections; 2) to evaluate the safety and tolerability of inhaled zanamivir compared to placebo in the treatment of influenza A and B viral infections; 3) to evaluate the efficacy, safety and tolerability of inhaled zanamivir compared to placebo in the treatment of influenza A and B viral infections in "high risk" patients; and 4) to assess the impact of treatment of influenza A and B viral infections with zanamivir on patient productivity and healthcare resource use.

**Technical Approach:** This is a double-blind, randomized, placebo-controlled, parallel-group, multicenter study. All study subjects will receive study medication twice daily for five days. The first dose will be administered at the First Treatment Visit (Day 1). Subjects will attend a Post-Treatment Visit (Day 6) on completion of study treatment and a Follow-up visit on Day 28. Subjects will also be contacted by telephone on Day 3 (during treatment) and day 14 (on completion of the first diary card). Subjects will maintain a diary with symptom assessment, adverse event and concomitant medications. Safety evaluations will include lab analyses of blood (hematology and biochemistry) and clinical adverse event inquiries. Prior to initiating the treatment trial, Madigan will participate in a surveillance study to identify the presence of the influenza virus in the community. Patients will be consented with a short surveillance study form and a throat swab will be performed.

**Progress:** Protocol is awaiting final approval from CIRO to start.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/021		<b>Status:</b> Completed	
<b>Title:</b> Comparison of Currently Available Oropharyngeal Suction Systems vs. New Large Diameter System in Time to Intubation					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Nov 96		
<b>Department:</b> Emergency Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT James T. Vandenberg, MC					
<b>Associate Investigators:</b>			CPT Robert H. Lutz, MC		
<b>Key Words:</b> Suction systems, oropharynx, intubation					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

Study Objective: To test and compare three different suction systems to determine which arrangement is most efficient for oropharyngeal suctioning and as a aid to intubation.

Technical Approach: We plan to test the two currently available hospital suction systems and a third, new large diameter system designed to improve evacuation time of chunky vomitus. Standard hospital wall suction with a vacuum pressure of -500 mm Hg, Ohmeda regulators, and 1500cc reservoir containers will be used with all the setups. Two of the suction arrangements will use standard 1/4 inch suction tubing attached to a suction canister. One will use a standard blunt nosed yankauer tip while the other will use an open bore yankauer tip. (1/4 inch ID). The new large diameter system will use 3/4 inch ID tubing and a 5/8 inch open bore tip. The results of our prior study demonstrated evacuation time of viscous or particulate material is greatly reduced with a large diameter suction system but practical applicability of using the large diameter system has not been demonstrated. The efficacy of suctioning water, activated charcoal, and simulated particulate vomitus will be measured by the time it takes to clear the oropharynx of a volunteer. Analysis of variance will be used to compare the times.

Progress: Project is complete.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/127		<b>Status:</b> On-going
<b>Title:</b> Efficacy of Clonidine for Prophylaxis of Acute Mountain Sickness				
<b>Start Date:</b> 07/18/97		<b>Est. Completion Date:</b> Oct 98		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Ian S. Wedmore, MC				
<b>Associate Investigators:</b>		CPT Alexandre F. Migala, MC		
<b>Key Words:</b> Mountain sickness, clonidine, placebo				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: A double blind placebo controlled study to determine if clonidine is effective in preventing or reducing the incidence of acute mountain sickness (AMS).

Technical Approach: Climbers will take a study drug dose the night prior to climbing and BID thereafter until returning to sea level. ESQs will be completed at sea level, 6000 ft, 10000 ft, and 14400 ft elevations. These will be completed 15 minutes after arrival at each altitude. Should the climb be terminated due to weather or any other objective condition preventing arrival at the summit, an ESQ will be conducted at the high point obtained. Four doses of study drug will be utilized, this will allow drug to be started 12 hours prior to beginning the climb and continued on a q12 hour basis until the completion of the climb. Results of the ESQs will be analyzed to determine if subjects meet criteria for AMS.

Progress: 10 subjects have been entered in FY 97.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF FAMILY PRACTICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/018	<b>Status:</b> Completed
<b>Title:</b> Biomechanics of the A2 Flexor Tendon Pulley in A Climbing Position Cadaver Model: Effects of Circumferential Taping		
<b>Start Date:</b> 12/19/96	<b>Est. Completion Date:</b> Dec 96	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Peter J. Benson, MC		
<b>Associate Investigators:</b> A. Bach MAJ Winston J. Warme, MC	LTC D. E. Casey Jones, MC A. Tencer CPT Clark P. Searle III, MC	
<b>Key Words:</b> A2 Flexor tendon pulley: climbing position, circumferential taping		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: (1) To determine the incidence of hematuria in a young healthy population. (2) To determine the effect of routine exercise such as the APFT on urinalysis for blood and protein. (3) To modify a guideline for assessment of painless hematuria after routine exercise.

Technical Approach: The purpose of this study will be to identify the incidence of exercise-induced hematuria secondary to routine physical training and develop guidelines for proper urine collection and triage of patients found to have hematuria after exercise. 500 male and female ROTC Cadets will be recruited during routine physical examinations which includes a urinalysis. A questionnaire will be completed and urine will be collected following a standard APFT. Urinalysis will check for blood and protein. If positive for blood, the specimen will be forwarded for microscopic study to determine if >3 RBC/HPF are present. If so, the participant will be asked to provide specimens at 24 hrs, 48 hrs, 72 hrs, and 1 week after the APFT. The data will be collected and analyzed as part of a descriptive study.

Progress: Manuscript being prepared.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/127		<b>Status:</b> On-going	
<b>Title:</b> Incidence of Exercise Induced Hematuria After the Army Physical Fitness Test (APFT)					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Aug 96		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Yong H. Chun, MC					
<b>Associate Investigators:</b>			MAJ Charles Payne, MC		
<b>Key Words:</b> Hematuria, exercise-induced, APFT					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

Study Objective: (1) To determine the incidence of hematuria in a young healthy population. (2) To determine the effect of routine exercise such as the APFT on urinalysis for blood and protein. (3) To modify a guideline for assessment of painless hematuria after routine exercise.

Technical Approach: The purpose of this study will be to identify the incidence of exercise-induced hematuria secondary to routine physical training and develop guidelines for proper urine collection and triage of patients found to have hematuria after exercise. 500 male and female ROTC Cadets will be recruited during routine physical examinations which includes a urinalysis. A questionnaire will be completed and urine will be collected following a standard APFT. Urinalysis will check for blood and protein. If positive for blood, the specimen will be forwarded for microscopic study to determine if >3 RBC/HPF are present. If so, the participant will be asked to provide specimens at 24 hrs, 48 hrs, 72 hrs, and 1 week after the APFT. The data will be collected and analyzed as part of a descriptive study.

Progress: Data collection was finished in FY 96, still awaiting data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/056	<b>Status:</b> Completed
<b>Title:</b> Incidence of Unintended Pregnancy in Female Soldiers Presenting to OB Orientation at Madigan Army Medical Center From March 1996 to February 1997		
<b>Start Date:</b> 02/16/96	<b>Est. Completion Date:</b> Feb 97	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Jeffrey B. Clark, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Pregnancy:unintended, female soldiers		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** (1) To determine the incidence of unintended pregnancy in active-duty females presenting to OB orientation. (2) To determine if the soldier was using contraception if the pregnancy was unintended. (3) To determine if the soldier was using the method of contraception correctly. (4) To determine why a contraception was not being used if the pregnancy was unintended.

**Technical Approach:** Pregnant soldiers will be surveyed during MAMC OB orientation. Participants will complete the questionnaire, and return it to the OB orientation coordinator. The following information will be analyzed using descriptive statistics: (1) Demographic characteristics of the respondents by age, grade, marital status, and race, (2) Frequency of unintended pregnancy both total and stratified (3) Frequency of unintended pregnancy in those not using contraception or using it incorrectly.

**Progress:** The sample consisted of 261 (75) junior enlisted soldiers, 50 (15%) noncommissioned officers, and 36 (10) officers. Overall, 55% of soldiers reported that pregnancy was unintended. The majority of officers (60%) and noncommissioned officers (65%) reported that pregnancy was intended. In contrast, only 39% of the junior enlisted soldiers reported that pregnancy was intended. The majority (62%) of women reported that they were not using any form of birth control during the month they conceived. The most common reason for not using contraceptive devices was because of side effects. The most common contraceptive methods reported was the male condom. Prevention programs should target the junior enlisted soldiers and address knowledge, attitudes, and beliefs related to the use of contraception.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/022		<b>Status:</b> Terminated	
<b>Title:</b> Healing of Stress Fractures and Shin Splints Using Non-thermal, Pulsed High Peak Power, High Frequency, Electormagnetic Energy Therapy					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard T. Dombroski, MC					
<b>Associate Investigators:</b> CPT Robert C. Ladd, MC LTC Marc G. Cote, MC			LTC Richard A. Sherman, MS LTC John M. Bauman, MC Jerome Billingsley, M.D.		
<b>Key Words:</b> Pulsed electromagnetic fields, stress fractures, shin splints					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine whether application of non-thermal, pulsed high peak power, high frequency, electromagnetic energy (PEMF) over the stress fracture of shin splint site used in conjunction with standard therapeutic approaches, reduced the amount of shin pain and increases endurance on the treadmill in relation to those receiving standard treatment with placebo PEMFs.

**Technical Approach:** A previous double blind placebo controlled pilot study (by LTC Sherman, the co-principal investigator of this study) of Army basic trainees diagnosed with either tibial or metatarsal stress fractures showed that the use of PEMF returned the soldier to full duty an average of one week before those treated with placebo PEMFs. This study did not have adequate outcome measures because a wide variety of health care providers used differing criteria for sending soldiers back to duty.

We propose a similar design of a double-blind placebo controlled study. The study group will receive the standard treatment in addition to the PEMF or placebo. Prior to initial exposure a treadmill will be used to evaluate pain and endurance thereby creating a more standardized method to measure outcome. Subjects will be stratified by grade of the stress fracture based on the bone scan and then will be randomly assigned to either the placebo or the PEMF group. Subjects with shin splints will be randomized without stratification. This will be an entirely double-blind study as the subjects will not be able to tell which group they are in because the PEMF generator sounds the same in both the stand-by (placebo) and the functional modes. Patients cannot feel the device operating. The technician who operates the device will know which group the subject is in but the technician and physicians doing the evaluations will have no idea which group the patients are in. The treadmill test will be repeated at the end of the two week exposure period. A power analysis of the study results reported shows that 33 subjects will be needed in each group for each diagnosis assuming that (a) we predict the PEMF group will do better (one-tailed test) and (b) an 80% chance of finding a difference between the two groups at a 0.05 level of significance. Thus a total of about 132 subjects will be required.

**Progress:** This study was terminated due to insufficient eligible patients. Five patients completed the study without significant change in shin splint symptoms. A significant factor in the decision to terminate the protocol is the nonportability of the machine.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/050		<b>Status:</b> On-going	
<b>Title:</b> Unintended Pregnancy Prevention Program					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Diane M. Flynn, MC					
<b>Associate Investigators:</b>			LTC Jeffrey D. Gunzenhauser, MC		
LTC Roderick T. Hume Jr., MC			Ann K. Lancaster, CHN		
LTC Jeffrey B. Clark, MC					
<b>Key Words:</b> Pregnancy:prevention, Pregnancy:unintended					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

Study Objective: The purpose of this study is to evaluate the effect of an intervention consisting of education and facilitated access to contraception on the unintended pregnancy rate of active duty US Army soldiers serving at Ft Lewis, WA.

Technical Approach: This research project is a randomized clinical trial designed to determine the effect of education and facilitated access to contraception on unintended pregnancy rates among female soldiers at Ft Lewis. Effectiveness of the intervention will be determined by: 1) Calculating annualized pregnancy rates using SIDPERS data and positive beta-HCG results from the MAMC clinical laboratory; unintended pregnancy rates will be determined from a survey completed at prenatal care orientation. 2) A questionnaire mailed to women in the Intervention Group and the Control Group one year after the intervention designed to assess contraception use, whether the intervention affected contraception use, and the rate of unintended pregnancy.

Progress: 12 subjects have been entered, all in FY 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/079		<b>Status:</b> Completed	
<b>Title:</b> Operational Medical Database Investigation					
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Mark D. Harris, MC					
<b>Associate Investigators:</b>			LTC Brian R. Johnson, MC		
<b>Key Words:</b> Database:medical					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97	

**Study Objective:** 1) To discover what primary care doctors are currently using for a medical database in operational environments. 2) To discover what primary care physicians believe are the characteristics of the perfect operational medical database.

**Technical Approach:** One thousand male and female active duty Army, Navy and Air Force family practitioners and GMOs between the ages of 20-65 will be recruited. We plan to first create an operational medical database questionnaire to use as a pretest questionnaire with members of the MAMC Department of Family Practice. Once the protocol is approved, we will mail out a final questionnaire. Respondents will answer anonymously, but will return a separate, included card to indicate when they have returned the survey so that I know who has returned one. A second survey will be sent to those from whom I have not received a completed survey. Three to four months after the initial mailing, data will be tabulated, analyzed, presented and published.

**Progress:** Of 740 surveys delivered, 445 (60%) were returned. Currently 96% of responding primary care physicians use books, 37% use journals, and 11% use computer software in their medical reference database. Of those now using books, 72% were satisfied, compared to 61% of those using journals and 45% of those using software. The most common book used was the Merck Manual. The most important characteristics desired in a field medical database were broad coverage, ease of use, and light weight. The majority of respondents believe that a good medical reference database is important, but that current medical databases limit the quality of medicine that they practice in the field.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/048		<b>Status:</b> On-going
<b>Title:</b> The Impact of Flowsheets on the Delivery of Preventive Care				
<b>Start Date:</b> 02/21/97		<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Family Practice		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Franklin H. Hauger, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Preventive Medicine, flowsheets, reminder, tracking				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** To assess the impact of a flowsheet reminder system on the delivery of preventive care services such as mammograms, Pap smears, immunizations, and cholesterol screening in a family practice clinic.

**Technical Approach:** Plan to review the charts of 250 family practice empaneled patients and compare the rate of compliance with recommendations of the delivery of immunizations (DPT, OPV, MMR, and dT), breast exams, mammograms, Pap smears, testicular self exam counseling, diet/exercise counseling, and cholesterol screening. I will compare these rates from the 3 year period prior to the initiation of the flowsheet reminder system to the rates from the 3 subsequent years.

**Progress:** Two hundred and forty-four charts were reviewed. The principal investigator was transferred before protocol completion and he has been unable to analyze the data at his new station.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/149	<b>Status:</b> On-going
<b>Title:</b> Primary Prevention of Otitis Media Using a Parental Education Model to Reduce Risk Factors		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b>	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LCDR Robert C. Marshall, MC USNR		
<b>Associate Investigators:</b> LT Joan Morris, NC USN		
LT Mark Flynn, MC USNR		
<b>Key Words:</b> Otitis media, education		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** The objective of this study is to reduce the incidence of acute otitis media by educating parents to modify known risk factors.

**Technical Approach:** All infants born at Naval Hospitals Bremerton and Oak Harbor for the month of April, May, June and July 1995 will be screened for exclusion criteria or Tri-care assignment to primary care portal outside of USNH Bremerton or Oak Harbor. If acceptable, the patient will be stratified and randomized to intervention and control groups. Each infant will be given a random number derived from a random number table. The control group will receive usual information on child care. In addition to this information, the intervention group will also receive a parental handout on risk factor modification of known behaviors that increase the risk of otitis media and a 10-15 minute talk by a nursery nurse or corpsperson about modifying these factors. All parents will complete a newborn risk factor questionnaire. At each well baby visit, ER visit and acute clinic visit, the child will be evaluated for otitis media using published criteria for diagnosis and a check-off sheet. Parents and infants in both groups will receive only routine care and counseling subsequent to the initial encounter. Follow-up questionnaires will be mailed at 6 and 12 months.

**Progress:** All subjects have been entered. The study is now in the follow-up stage.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/177		<b>Status:</b> Completed	
<b>Title:</b> Comparison of Manipulative Treatment and Conservative Measures in the Management of Carpal Tunnel Syndrome (CTS)					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Family Practice			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT David C. Martin, MC					
<b>Associate Investigators:</b> LTC Brian R. Johnson, MC R.K. Evans			COL Shashi J. Kumar, MC CPT Mary V. Biglow, MC		
<b>Key Words:</b> Carpal tunnel syndrome, manipulation, home exercise program					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		12/19/96	

**Study Objective:** The objective of this study is to show that manipulation of the wrist and/or the thoracic outlet in combination with a home exercise program can alter the symptoms, function and/or nerve conduction latencies in carpal tunnel syndrome. It will be a prospective, randomized, controled and partially blinded clinical trial.

**Technical Approach:** The subjects for the study will be consecutively drawn from a pool of patients referred to the Madigan Physical Medicine Department. All patients with suspected CTS will be given nerve conduction studies by the same physiatrist (S.K.). The patients with abnormal nerve conduction studies will be asked to enroll. All enrollees will be evaluated for level of function and mobility by an independent blinded investigator (D.M.) at the start and end of the study period. They will fill out questionnaires for demographic information, pain level, mobility and function. The individuals will be randomly assigned to the treatment or control group and will be blinded as to which group they are in. All subjects will be seen by the same physician (B.J.) weekly for the first month and every other week for the next two months for a total three month study period. At each visit, the control group will be asked to fill out pain scales and will be evaluated for range of motion. The treatment group will be asked to fill out pain scales and then treated using osteopathic methods (Sucher, 1993, 1995). The treatment group will also be instructed in a home exercise program. In addition to a final evaluation by D.M., each participant will be asked to fill out the questionnaires again and will be given repeat nerve conduction studies by the same physiatrist (S.K.) who will also be blinded.

**Progress:** Seven patients were enrolled and three dropped out. Patient enrollment is complete. The investigator is now in the process of analyzing the data.

### Detail Summary Sheet

Detail Summary Sheet					
Date: 30 Sep 97		Protocol No.: 96/130		Status: Completed	
Title: Determining the Need for Teaching Interns About Professional Boundaries in the Physician-Patient Relationship					
Start Date: 06/21/96			Est. Completion Date: Jul 96		
Department: Family Practice			Facility: MAMC		
Principal Investigator: LTC William F. Miser, MC					
Associate Investigators: LTC David C. MacDonald, MC			COL Paul Evans, MC		
Key Words: Physician, Patient relationship, professional boundaries, training					
Accumulative MEDCASE Cost:		\$0	Est. Accumulative OMA Cost:		\$0.00
			Periodic Review:		9/30/97

**Study Objective:** We want to know if interns have received any training during medical school on professional boundaries in the physician-patient relationship. The information obtained from this study will be the basis for the development of an educational curriculum dealing with these topics.

**Technical Approach:** This is a one-time, cross-sectional survey. During the initial orientation this academic year, the Directors of Medical Education at each military training institution will distribute an anonymous questionnaire to a total of approximately 750 interns among the various sites. The questionnaire and the resulting educational curriculum will address several issues in the physician-patient relationship to include (1) romantic or sexual relationships between a physician and a patient, (2) what to do with a seductive patient in the office, (3) what to do if they feel sexually aroused by a patient, and (4) the use of chaperones in patient care. We also want to explore their attitudes toward dating or having sexual relationships with current and former patients. Finally, we want to know if they have ever had a patient make a sexual advancement toward them as a medical student, and if, when in medical school, they knew of any medical student, residents, or attendings who had a sexual relationship with a patient. The interns will be allowed to ask questions dealing with the survey which will not be identified with the respondents.

**Progress:** Of 568 surveys distributed, there were 442 (78%) responses. Respondents were 78% men, 58% married, and 38% never married, single from 87 medical and 14 osteopathic schools from 37 states. 58% were unaware of the AMA standards. Of those, 30% did not understand them.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/101		<b>Status:</b> On-going
<b>Title:</b> Postresidency Army Family Practice Inpatient Care and Implications on Residency Training				
<b>Start Date:</b> 06/20/97		<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> Family Practice		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Eric D. Morgan, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Residency training, family practice, inpatient care				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: 1) To describe what family practice inpatient work is being done after residency; 2) to describe what inpatient work is being done at residency training locations; and 3) to identify clinically significant differences between post-residency sites and medical center based training and community hospital based training programs.

Technical Approach: Family practice residency involves three intensive years of training to learn and master the breadth of hospitalized and ambulatory medical practice. Training programs are supposed to simulate what graduates encounter after completing residency. This information can derive from anecdotes, impressions, surveys or descriptive studies. There have been no formal descriptive studies in over 10 years evaluating what inpatient care family practitioners are involved in. During this same time period, inpatient medicine has changed substantially. Multicenter retrospective descriptive study generated from chart reviews of approximately 1000 charts from each broad training category of USA MEDDAC post-residency sites, medical center based FP training sites, and community hospital based training FP sites. Data is also reviewed that had been collected, but not previously published, from Fort Sill in the mid-1980s. Descriptive statistical analysis will be performed on data from each site. Residency and post-residency sites are then compared with each other utilizing chi-square analysis. Post-residency sites are similarly compared to historical data from the mid-1980s to demonstrate trends in Army family practice care. Study should objectively demonstrate trends in Army post-residency family practice inpatient care. It should also demonstrate what care the residency training programs are actually involved in. This study will identify priority areas of inpatient training. Areas involving misallocation of resources will also be identified. This will permit better allocation of family practice training time and resources to pertinent inpatient problems.

Progress: 1,750 subjects were entered during FY 97. Data analysis is still pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/053	<b>Status:</b> Completed
<b>Title:</b> The Annual Pap Smear Screen: Knowledge by Women Soldiers		
<b>Start Date:</b> 01/19/96	<b>Est. Completion Date:</b> Dec 96	
<b>Department:</b> Family Practice	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Heidi P. Terrio, MC		
<b>Associate Investigators:</b> LTC William F. Miser, MC                      LTC Donald M. Bradshaw, MC LTC Jeffrey D. Gunzenhauser, MC		
<b>Key Words:</b> Pap smear, annual, women soldiers		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** (1) To determine the number of active duty women who comply with regulations by receiving an annual Pap smear. (2) To determine factors influencing active duty Pap smear screening. (3) To compare the cervical cancer risk factor differences between women who have/have not received an annual Pap. (4) To compare age-specific atypia rates to their reported history of risk factors as indicated on the questionnaire for those women who have had a Pap at Fort Lewis. (5) To determine the percentage of women who know if their Pap had abnormality. (6) To determine the sexual behavior of women soldiers, their average number of sexual partners, the percentage that are in a monogamous relationship, the types of contraception that are used, and the percentage who obtain an elective termination of pregnancy.

**Technical Approach:** SIDPERS database will be used to identify all active duty women on Fort Lewis stationed at all units except the AMEDD units. Of the approximate 2100 active duty women from field units, 600 of these women will be age stratified, then randomly selected by a computer program. Survey will be sent to their unit address. COPATH database from MAMC cytology section will be used to confirm Pap smear in the last year and abnormality for those who had their Pap smear at Fort Lewis. We will also correlate the risk factors of the sample of women who have had their pap at MAMC to their cytologic and pathology results dating as far back as Oct 92 when the COPATH database began. Descriptive statistics will be used for demographic data, access to care information and risk factor data. In the evaluation of risk factors between the two groups of women, the women who have attained an annual Pap versus those who have either not had a Pap or who have not had one in greater than a year, multivariate analysis will be used, as well as, a one tailed t-test for a comparison of the cumulative score between the two groups. Chi-square analysis will be employed in the analysis of assessing the knowledge of abnormality of their own Pap smear.

**Progress:** The study was complete in June 1996. In FY 97, the work consisted of data management and analyses. There are manuscripts that were sent to USAFP and AAFP. The Journal of Family Practice has offered to publish the first place award winning paper but I have not sent them the manuscript because there was some last minute analyses used for the presentation that were not included in the paper.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/090		<b>Status:</b> On-going
<b>Title:</b> Treatment of Nocturnal Leg Muscle Cramps: A Double-Blind Placebo-Controlled Crossover Trial of Magnesium Oxide				
<b>Start Date:</b> 04/19/96		<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> Family Practice		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Bruce A. Woolman, MC				
<b>Associate Investigators:</b> CPT John P. Barrett, MC		MAJ Alan J. Barker, MC		
<b>Key Words:</b> Muscle:nocturanl cramps, muscle:leg, magnesium oxide				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		05/16/97

Study Objective: To determine the effectiveness of magnesium oxide in reducing or eliminating nocturnal leg muscle cramps when compared to placebo.

Technical Approach: No current pharmacologic agent is approved for use in the treatment or prevention of nocturnal leg muscle cramps. Quinine appears to be an effective remedy but sufficient evidence for its efficacy and safety are lacking. Magnesium supplementation has been given trial in Europe for the treatment of night leg cramps. No studies have been done in this country to assess the efficacy of magnesium. Patients with a history of nocturnal leg muscle cramps and who are experiencing 2 or more cramps per week will be considered for enrollment in this study. Patients will be primarily identified from Family Practice Clinic physician panels with open invitation to other interested patients who are eligible DOD beneficiaries not followed in MAMC FP Clinic. Subjects will be observed via a 2 week symptom diary prior to treatment for 2-weeks with either magnesium oxide or placebo. During the full four weeks of the study, patients will keep a daily symptom diary that will be given to one of the investigators at each clinic visit. These symptom diaries will record the number, severity and duration of muscle cramps experience. The data obtained will be analyzed for statistical significance.

Progress: 4 subjects have been entered in FY 97.



### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol No.:** 96/150      **Status:** Completed

**Title:** Characteristics of Outstanding Teachers of Primary Care Medicine in the U.S. Military

**Start Date:** 08/16/96      **Est. Completion Date:** Dec 96

**Department:** Family Practice      **Facility:** MAMC

**Principal Investigator:** COL Joseph F. Yetter III, MC

**Associate Investigators:** None

**Key Words:** Teachers, Primary Care Medicine, Military

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0	OMA Cost: \$0.00	9/30/97

**Study Objective:** To determine the characteristics of outstanding teachers of primary care medicine in the U.S. military.

**Technical Approach:** We will send a letter and a survey form to each chief of each department of primary care (Family Practice, Internal Medicine, and Pediatrics) at every Army, Navy, and Air Force teaching hospital where there are residency programs in their respective specialties. The letter introduces the research project, requests surveys be given to these teachers, and explains that we will request the name of the outstanding teacher later. Two months later, we will send follow-up letters to the same chiefs of departments, requesting the name of the outstanding teacher, as well as additional information and participation by teaching chiefs and chief residents. For each selected outstanding teacher, two controls will be randomly selected from the list of physicians from the same department. All responses will be added into a data base without designation as outstanding teacher or control. Responses of the selected outstanding teachers will be compared with the responses of the controls.

**Progress:** 163 faculty members from 42 residency programs participated. Of all the characteristics of outstanding teachers, faculty development training is the distinctive, important, modifiable, characteristic of Family Practice faculty that is associated with selection as outstanding teacher of the year. Faculty development training ought to be encouraged and supported by teaching programs in Family Practice and should be considered in other training programs.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,  
CARDIOLOGY SERVICE**

### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol No.:** 96/069      **Status:** On-going

**Title:** Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

**Start Date:** 02/16/96

**Est. Completion Date:** Mar 01

**Department:** Medicine/Cardiology

**Facility:** MAMC

**Principal Investigator:** MAJ Maureen A. Arendt, MC

**Associate Investigators:**

COL Roger F. Chamusco, MC

MAJ Herman E. Collier III, MC

MAJ Michael D. Eisenhauer, MC

MAJ James P. Olson, MC

MAJ Patrick A. Cambier, MC

LTC Alice M. Mascette, MC

LTC Karl C. Stajduhar, MC

CPT John A. McHenry, MC

CPT Thomas M. Roe, MC

**Key Words:** Atrial fibrillation, drug therapy, heart rate control, heart rhythm control

**Accumulative**

**MEDCASE Cost:**

\$0

**Est. Accumulative**

**OMA Cost:**

\$0.00

**Periodic Review:**

02/21/97

**Study Objective:** 1) To compare whether optimized antiarrhythmic drug therapy administered to attempt to maintain sinus rhythm has an impact on total mortality when compared to optimized therapy which controls the heart rate. 2) Since stroke is such an important endpoint in trials of patients with atrial fibrillation, composite endpoints will include the following: total mortality, disabling stroke or anoxic encephalopathy, major bleeding and cardiac arrest; cost; quality of life.

**Technical Approach:** This is a multi center trial sponsored by the National Heart, Lung, and Blood Institute. The purpose is to compare the effect on survival of two different treatment plans in patients with atrial fibrillation. One treatment is aimed at rate control and the other at maintaining a normal sinus rhythm. The primary physician will choose which drug or drugs are used to obtain each treatment objective. The physician will initially determine the treatment to convert patients to normal sinus rhythm after which the patient will be randomized to one of the treatments described above. Patients will be followed at month 2 and 4 and then at least every 4 months until the year 2001. Patients will complete a quality of life questionnaire and have an assessment of their functional status completed at various time points. Patients who fail their assigned treatment or are intolerant will continue to be followed regardless of crossover to another therapy. We anticipate enrolling 15 patients at Madigan Army Medical Center.

**Progress:** 9 subjects were entered in FY 97, for a total of 12 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/068		<b>Status:</b> Completed	
<b>Title:</b> A Double-Blind, Placebo Controlled, Randomized, Dose Response Study of Oral dl-Sotalol Hydrochloride for the Maintenance of Sinus Rhythm in Subjects with Prior Symptomatic Atrial Fibrillation or ....					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Maureen A. Arendt, MC					
<b>Associate Investigators:</b>					
COL Roger F. Chamusco, MC			MAJ Patrick A. Cambier, MC		
MAJ Herman E. Collier III, MC			LTC Alice M. Mascette, MC		
CPT Michael A. Rave, MC			LTC Karl C. Stajduhar, MC		
CPT Scott A. Sample, MC			MAJ Mark E. Peele, MC		
CPT Thomas M. Roe, MC			MAJ James P. Olson, MC		
			MAJ Michael D. Eisenhower, MC		
<b>Key Words:</b> Sinus rhythm, atrial fibrillation, dl-Sotalol Hydrochloride					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		06/21/96	

**Study Objective:** To evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm.

**Technical Approach:** Multicenter, double-blind, placebo controlled, randomized, dose response study to evaluate the efficacy and safety of oral dl-sotalol Hcl in subjects with prior symptomatic atrial fibrillation (AFIB) or atrial flutter (AFL) for the maintenance of sinus rhythm. Six subjects will be randomly assigned to receive one of the three fixed dose regimens of dl-sotalol Hcl (80 mg, 120 mg or 160 mg) or placebo administered every 12 hours orally. The study will consist of double-blind and open-label phases. Treatment will last for 12 months. In the analysis of time to AFIB/AFL, the log-rank test will be used. The proportions of subjects free of AFIB/AFL for two treatments groups will be compared at 6 months and 12 months using the product-limit estimates. The corresponding variances will be computed using Greenwood's formula. This method adjusts for dropouts or censored data.

**Progress:** This study was closed to patient entry in June 1997 due to sufficient accrual of patients. Fifteen (15) patients were consented and randomized at Madigan; 14 patients completed the study and one patient was dropped from the study due to bradycardia. One adverse event, which was not study related, occurred at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/142		<b>Status:</b> On-going	
<b>Title:</b> A Parallel Dose-Response Study of Sustained-Released Moxonidine in Patients with Congestive Heart Failure					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Maureen A. Arendt, MC					
<b>Associate Investigators:</b>			LTC Alice M. Mascette, MC		
MAJ Karen A. Hicks, MC			MAJ James P. Olson, MC		
LTC James J. King, MC			MAJ David T. Schachter, MC		
CPT Kenneth M. LeClerc, MC			CPT Allan B. Wicks, MC		
MAJ Steven E. Miller, MC			MAJ Theresa A. Horne, AN		
<b>Key Words:</b> Congestive Heart Failure, moxonidine, norepinephrine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		<b>9/30/97</b>	
\$0		\$0.00			

**Study Objective:** To evaluate the dose-related change in plasma norepinephrine from baseline to 4 hours post dose after approximately 19 weeks of therapy with placebo or SR moxonidine (up to 1.5 mg BID) in patients with NYHA Class II-IV CHF.

**Technical Approach:** This is a randomized, placebo-controlled, parallel dose response, multicenter study in patients with congestive heart failure (NYHA Functional Classes II-IV). Each patient's study duration will be approximately 23 weeks, consisting of five phases: Screening, Baseline/Randomization, Dose Optimization, Dose Maintenance and Study Drug Washout. The study is double-blind during the Dose Optimization and Maintenance Phases, and is single-blind during the Placebo Run-In, Baseline, and Study Drug Washout Phases. Doses will be increased at 1 week intervals by 0.3 mg BID until the patient reaches the randomized or maximum tolerated dose (whichever is less). During Dose Optimization, if a patient experiences significant blood pressure reduction, symptomatic hypotension, or other symptoms of intolerance, the dose can be maintained or reduced rather than increased as per protocol. The randomized or maximally tolerated dose will be maintained for a minimum of 12 weeks. Following maintenance phase, patients will receive placebo during a 2-week study drug washout period. Patients will be seen for a screening and then baseline visit, weekly during the 7-week dose optimization period, 4 times during the 12-week maintenance period, and then 2 weeks after study drug washout. Safety assessments will include adverse event questioning, physical exams, ECG and Holter monitor at selected time points, and laboratory tests.

**Progress:** Not started, protocol is awaiting CIRO approval.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/024		<b>Status:</b> Completed	
<b>Title:</b> A Randomized, Open-Label, Active-Controlled, Multicenter Phase III Safety Study of Two Doses of NATRECOR hBNP Administered As A Continuous Infusion in the Treatment of Decompensated CHF					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Maureen A. Arendt, MC					
<b>Associate Investigators:</b>			MAJ David T. Schachter, MC		
LTC Karl C. Stajduhar, MC			LTC Alice M. Mascette, MC		
MAJ James P. Olson, MC			MAJ Karen A. Hicks, MC		
CPT Allan B. Wicks, MC			MAJ Steven E. Miller, MC		
CPT Kenneth M. LeClerc, MC					
<b>Key Words:</b> Heart Failure, decopensated, NATRECOR-hBNP					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>9/30/97</b>

**Study Objective:** To gain additional safety and clinical experience with NATRECOR® hBNP in the treatment of decompensated CHF requiring inpatient parental vasoactive therapy.

**Technical Approach:** This is a phase III multicenter study enrolling approximately 300 subjects with symptomatic, decompensated CHF for whom inpatient parenteral vasoactive therapy is deemed appropriate. Eligible patients will be randomized to one of three treatment groups: Group 1 - NATRECOR® hBNP 0.015 µg/kg/min, Group 2 - NATRECOR® hBNP 0.03 µg/kg/min, Group 3 - a standard care agent. NATRECOR® hBNP will be administered intravenously as a loading bolus followed by a fixed-dose infusion. The standard care agent will be a single parenteral vasoactive agent routinely used for the short-term management of decompensated CHF, such as intravenous nitroprusside, nitroglycerine, dobutamine, or milrinone. Treatment assignment will be open-label with regard to the standard care versus NATRECOR® hBNP; for NATRECOR® hBNP subjects, assignment to the two dose groups will be double-blinded. The duration of the therapy with the initial study drug will vary according to each patient's cardiopulmonary status as determined by the attending physician. For any subject who is not responding adequately to the initial study drug or who is experiencing a worsening of their CHF, a second parenteral vasoactive agent may be added to - or substituted for - the initial study drug. Clinical status and adverse events will be followed. Blood samples for assessment of serum anti-BNP antibodies will be obtained at baseline and at Day 21 for subjects receiving NATRECOR® hBNP. Also at Day 21, each subject's clinical course will be reviewed with regard to mortality status, duration of initial hospitalization, the need for re-admission, and the need for dialysis and intubation during the 21-day study period.

**Progress:** Enrollment was closed in Jul 97 due to sufficient accrual of patients. Five patients were consented and randomized at MAMC. Four of the five patients completed the study. All five patients received the study medication. There was one adverse event at MAMC. The PI concluded that there may be some relationship, direct or indirect, of the BNL administration to the ventricular dysrhythmia in a patient with end stage heart disease with preexisting substrate for this dysrhythmia. The event was properly reported to all concerned.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/007	<b>Status:</b> On-going
<b>Title:</b> Antiplatelet Therapy vs Lovenox plus Antiplatelet Therapy for Patients with an Increased Risk of Stent Thrombosis (ATLAST)		
<b>Start Date:</b> 10/18/96	<b>Est. Completion Date:</b> Nov 97	
<b>Department:</b> Medicine/Cardiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Karen A. Hicks, MC		
<b>Associate Investigators:</b>		
MAJ Maureen A. Arendt, MC	LTC Alice M. Mascette, MC	
MAJ David T. Schachter, MC	LTC Karl C. Stajduhar, MC	
COL Roger F. Chamusco, MC	CPT John A. McHenry, MC	
MAJ Michael D. Eisenhauer, MC	MAJ James P. Olson, MC	
CPT Kenneth M. LeClerc, MC	CPT Allan B. Wicks, MC	
	MAJ Steven E. Miller, MC	
<b>Key Words:</b> Stent thrombosis, Lovenox, placebo, ticlopidine, aspirin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	10/17/97

**Study Objective:** The primary objective is to demonstrate that a 14 day regimen of enoxaparin, compared to placebo, reduces the 30 day combined clinical endpoint incidence of death, non-fatal myocardial infarction and urgent revascularization, when each is added to the same concomitant antiplatelet regimen of ticlopidine (14 days) and aspirin ( $\geq 6$  mos) in patients at increased risk for stent thrombosis.

Secondary objectives include: 1. The comparative composite clinical endpoints at 14 days and 6 months after stent implantation. 2. The comparative incidence of major and minor hemorrhage and specified clinical laboratory changes and adverse events at day 14 (or within 48 hours after ending study-drug treatment) and Day 30 after stent implantation.

**Technical Approach:** This is a phase III, randomized, double-blind, multi-center, placebo-controlled, parallel group study. Immediately after sheath removal, following stent implantation during percutaneous intervention, eligible patients will be randomly assigned to receive either subcutaneous enoxaparin or matching placebo injections for 14 days, in addition to a concomitant oral antiplatelet regimen of aspirin and ticlopidine. Patients will have follow-up visits at days 5, 14, and 30 when labs will be drawn and they will be assessed for adverse events and clinical endpoints. A follow-up phone call will be made at 6 months.

**Progress:** 38 subjects were consented and 4 randomized during FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/140		<b>Status:</b> On-going	
<b>Title:</b> A Double-Blind, Placebo-Controlled, Parallel Design Study to Determine the Effect of 75 or 100 mg of Orally Administered Azimilide Dihydrochloride versus Placebo on Survival in Recent Post-MI....					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> May 99		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Alice M. Mascette, MC					
<b>Associate Investigators:</b>					
MAJ Karen A. Hicks, MC			MAJ Maureen A. Arendt, MC		
LTC James J. King, MC			MAJ James P. Olson, MC		
CPT Kenneth M. LeClerc, MC			MAJ David T. Schachter, MC		
MAJ Steven E. Miller, MC			CPT Allan B. Wicks, MC		
			MAJ Theresa A. Horne, AN		
<b>Key Words:</b> Post-MI, azimilide dihydrochloride, efficacy, mortality					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>9/30/97</b>

**Study Objective:** To evaluate the effects of 75 mg of azimilide dihydrochloride versus placebo or 100 mg of azimilide dihydrochloride versus placebo on all-cause mortality, based on longitudinal intent-to-treat observations in patients with a recent (within 6 to 21 days) acute MI, low left ventricular ejection fraction (15 to 35%), and low heart rate variability (£ 20 U). These patients are defined as "at high risk" of sudden death.

**Technical Approach:** This is a randomized, double-blind, placebo-controlled, multi-national study at approximately 500 study centers. A treatment regimen consisting of daily oral doses of 75 or 100 mg of azimilide dihydrochloride will be compared to a placebo group in a parallel design. Patients will be equally randomized across all 3 treatment groups. Patients who have recently experienced an acute MI and meet other study entrance and screening criteria will receive their first dose of study medication within 6-21 days of that MI. Once-daily treatment will be administered for approximately one year. No specific hospitalization is required for treatment. Screening procedures (to include a 24 hour Holter monitor) will be done to determine the group "at high risk" of sudden arrhythmic death. Evaluations during the treatment period will take place at Week 2, and at Months 1, 4, 8, and 12. Monthly serum pregnancy tests will be performed on females of childbearing potential who are not surgically sterile. Patients who complete 365 days of dosing will be followed for one month after completion of their participation in the study. Patients who withdraw from the trial early will return within 4 weeks for study exit procedures and furthermore, will be followed to assess survival status until the time at which they would have completed 365 day of dosing had they remained in the trial. Safety monitoring will include but is not limited to, clinical laboratory test results, 12-lead ECG measurements and frequency and severity of adverse events.

**Progress:** Study is awaiting CIRO approval to start.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/141		<b>Status:</b> Completed	
<b>Title:</b> A Phase II, Randomized, Open-Label, Multicenter, International, Angiographic Trial of the Efficacy of TNK-tPA Compared with Accelerated Activase Alterplase rt-PA in Acute Myocardial Infarction.....					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Alice M. Mascette, MC					
<b>Associate Investigators:</b> COL Roger F. Chamusco, MC MAJ Maureen A. Arendt, MC			W. Douglas Weaver, M.D. LTC Karl C. Stajduhar, MC CPT J. Olson, MC		
<b>Key Words:</b> Myocardial infarction, TNK-tPA, Activase Alterplase rt-PA					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The study is designed to determine the efficacy of TNK-tPA, a new thrombolytic agent, in the treatment of acute myocardial infarction, as compared with rt-PA. The primary objective of this study is to determine the percentage of subjects with TIMI grade 3 flow (normal, brisk blood flow) in the infarct-related artery (IRA) by angiography at 90 minutes after the start of treatment with bolus TNK-tPA (30 or 50 mg) compared with accelerated dosing of rt-PA (Activase-® Alteplase). Secondary objectives of this study are: 1) To evaluate IRA patency (TIMI grade flow and TIMI frame count) at 60, 75 and 90 minutes; 2) to evaluate the safety and clinical efficacy of TNK-tPA; 3) to evaluate the effects of TNK-tPA on coagulation and fibrinogenolysis; and 4) to evaluate the formation of antibodies against TNK-tPA.

**Technical Approach:** This is a phase II, randomized, open-label, multicenter trial designed to compare the efficacy of a new thrombolytic agent, recombinant TNK-tPA (two doses) versus a standard front-loaded infusion of rt-PA in the treatment of acute myocardial infarction. The primary endpoint is normal (TIMI 3) blood flow in the infarct related artery as judged by 90 minute angiography. Secondary objectives include evaluation of safety and efficacy of TNK-tPA, its effect on coagulation and fibrinogenolysis and antibody formation, and artery patency at earlier angiograms if performed. Concomitant therapy with heparin and aspirin will be given as per usual practice after thrombolytic therapy, and other medical therapy is at the discretion of the treating physician. Further intervention or revascularization is at the discretion of the treating physician. Blood samples for coagulation profiles, antibodies, and serum markers for myocardial damage will be drawn over the first 48 hours. A blood sample for antibody formation will be drawn on outpatient follow-up at 30 days; subjects who test positive for antibodies against TNK-tPA at 30 days will have an antibody sample repeated at 90 days.

**Progress:** Enrollment was discontinued by the sponsor in Mar 97 due to sufficient enrollment. Two patients were entered at MAMC. One patient received study medication.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/149		<b>Status:</b> Completed	
<b>Title:</b> ST Segment Depression in Localizing Regional Myocardial Ischemia in Unstable Angina					
<b>Start Date:</b> 08/16/96			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT John A. McHenry, MC					
<b>Associate Investigators:</b> LTC Vernon C. Parmley, MC Christopher Wolfe, M.D.			LTC Karl C. Stajduhar, MC Nora Goldschlager, M.D.		
<b>Key Words:</b> ST segment, depression, myocardial ischemia, angina					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

Study Objective: To determine if regional myocardial ischemia in unstable angina can be specifically localized based on the representative ECG leads demonstrating ST-segment depression.

Technical Approach: The major focus of this study is to determine whether labile ST-T wave depression in the setting of unstable angina can be used with any accuracy in localizing ischemic regions of myocardium threatened by impending infarction. Such repolarization abnormalities are known to not localize with exercise induced ischemia, but this has yet to be determined with certainty in the setting of unstable angina.

To evaluate this we anticipate enrolling a total of 200 patients in a 6 month period among three trial centers. Patients will be treated according to standard of care practice in the treatment of unstable angina. Patients considered to be high risk will undergo cardiac catheterization in the usual fashion.

ECG's showing labile ST segment depression during symptoms will be interpreted according to the myocardial segments they represent. Patients who additionally undergo coronary angiography will be entered into the study in the order of presentation with determinations then being made for coronary anatomy and the culprit vessel.

Interpretations of ischemic regions of myocardium, as determined by coronary anatomy and/or radionuclide scintigraphy, will be compared with ischemic regions determined by ECG criteria. Statistical determinations will then be made of the population makeup, coronary anatomy and the relation (if any) between the myocardial segments represented by the ECG's and the actual vessel involved.

Progress: Twenty patients were entered in FY 97 for a total of 55 subjects. Mean age of study patients was 52.5; 76% were male and 24% were female; 58% had anterior ST depression, 22% had lateral changes, and 15% had inferior changes.

Regional ST depression on the symptomatic ECG correlated significantly with the corresponding "culprit" artery in the setting of unstable angina. This was especially true with the LAD and its distribution with a positive predictive value of 91%. Negative predictive values were also found to be significant for all three major myocardial regions and their associated major epicardial artery.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/073		<b>Status:</b> On-going	
<b>Title:</b> Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Intracoronary Administration of High Osmolar Contrast Agents					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Steven E. Miller, MC					
<b>Associate Investigators:</b> MAJ Patrick A. Cambier, MC LTC Karl C. Stajduhar, MC			CPT Thomas M. Roe, MC Jacquelline Gillet, RN		
<b>Key Words:</b> Contrast agent, aminophylline, bradycardia, hypotension					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 05/16/97

**Study Objective:** The intent of this study is to determine whether the bradycardia and hypotensive response that is commonly encountered during intracoronary injection of high osmolar contrast agents can be prevented by intravenous aminophylline administration. A secondary objective is to determine whether intracoronary injection of high osmolar contrast agents ipsilateral to the origin of the sinus nodal (SA) artery leads to an increased incidence of bradycardia and hypotension.

**Technical Approach:** We intend to enroll 50-200 consecutive patients undergoing an elective cardiac catheterization. Patients will be consented at the time of their standard pre-catheterization appointment by the cardiac catheterization lab nurse. Patients will have orthostatic vital signs recorded to establish that they are euvolemic prior to receiving standard pre-catheterization medications. Standard cardiac catheterization procedures will be followed. After intraarterial access is obtained, baseline hemodynamic data will be recorded. Prior to the initial injection of contrast media, the patient will be randomized in a double blind fashion to receive either aminophylline 5 mg/kg IV over 5-10 minutes or the equivalent volume of saline placebo. A 15 second strip of the ECG and blood pressure will be recorded just prior to injection of contrast in both the left and right coronary arterial systems, and for one minute post injection. The pre-contrast heart rate and blood pressure, and minimum heart rate and blood pressure during contrast injection, will be determined. A comparison will be made between the absolute and percentage change in heart rate and blood pressure during contrast injection in the treated vs. placebo group. Also reported will be the need for additional therapies to treat hypotension and bradycardia (e.g. atropine, fluid boluses, need to change contrast agents, or the need for temporary pacing) in each group. The angiograms will be studied to determine the origin of the sinoatrial (SA) artery (left or right coronary artery). The data will be analyzed to determine whether intracoronary injection ipsilateral to the origin of the SA artery will manifest greater incidence of bradycardia and hypotension.

**Progress:** One new patient has been entered in FY 97 for a total of 30 patients entered. Randomization code remains unbroken in anticipation of entering more patients.

The principal investigator was changed from Dr. Karl Stajduhar in Jul 97. Dr. Stajduhar is now at BAMC where he is planning to submit protocol for approval in order to expand possible patient population.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/037	<b>Status:</b> On-going
<b>Title:</b> Impact of Aorto-Coronary Bypass Graft Markers on Graft Patency: A Prospective Trial		
<b>Start Date:</b> 12/15/95	<b>Est. Completion Date:</b> Jun 97	
<b>Department:</b> Medicine/Cardiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James P. Olson, MC		
<b>Associate Investigators:</b>		
MAJ Herman E. Collier III, MC	MAJ Patrick A. Cambier, MC	
LTC Blaine R. Heric, MC	LTC Alice M. Mascette, MC	
CPT Louis C. Coyle, MC	T.L. Eisenhower	
L. Snyder	Bonnie Goodman	
J. Carstens	MAJ Michael D. Eisenhower, MC	
<b>Key Words:</b> Grafts:aorto-coronary, patency		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/16/97

**Study Objective:** To address the impact of AOCCGM placement on graft patency in response to the widespread opinion that they may adversely affect graft patency.

**Technical Approach:** A power analysis has been performed to estimate required sample size. To detect a 10% adverse effect on graft patency, we estimate that 296 patients would be required, and to detect a 15% adverse effect, 132 patients would be required. Our sample size of 200 exceeds that needed to detect a 15% difference, and approaches that sample size needed to detect a 10% difference. Options include (1) extending the protocol for 6 months (if necessary after statistical evaluation has been completed for the first 200 cases), and (2) inviting BAMC to become involved with the protocol. All data will be compiled on a Microsoft EXCEL or ACCESS spreadsheet, allowing import or export of data to available software-statistical programs, including MacIntosh programs currently in use by MAMC's Department of Clinical Investigations. A weighted student's t-test will be performed to compare patency rates obtained from the 6-month angiography. Patient characteristics between the "marked" and "unmarked" (i.e.: experimental and control) groups will be compared with Chi-square testing. If profile characteristics are low in frequency, Fisher's Exact-testing will be substituted. P-values of <0.05 will be required to define statistical significance.

**Progress:** 38 subjects were entered during FY 97, for a total of 85 subjects (an additional 35 will be added from USN medical center at San Diego).

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/169		<b>Status:</b> Completed	
<b>Title:</b> A Multicenter, Randomized, Parallel, Double-Blind Study to Investigate the Safety and Clinical Efficacy of MK-383 Alone and MK-383 in Combination with Heparin vs. Heparin Alone in Patients with ....					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Dec 95		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Karl C. Stajduhar, MC					
<b>Associate Investigators:</b> LTC Alice M. Mascette, MC MAJ Herman E. Collier III, MC CPT J. Olson, MC MAJ Michael D. Eisenhower, MC			COL Roger F. Chamusco, MC MAJ Patrick A. Cambier, MC MAJ Maureen A. Arendt, MC CPT Thomas M. Roe, MC CPT John A. McHenry, MC		
<b>Key Words:</b> Myocardial infarction, MK-383, Heparin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** 1) To examine the efficacy of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in reducing the combined occurrence of the following clinical events: refractory ischemic conditions (refractory ischemia; hemodynamic instability; or severe, prolonged or repetitive anginal pain at rest requiring urgent invasive intervention within 12 hours of symptom onset), new myocardial infarction or death (through 7 days after initiation of study drugs) in high-risk patients with unstable angina/non-Q-wave myocardial infarction (UAP/NQWMI). the incidence of these endpoints will be examined at 48 hours, through 7 days after initiation of study drug, and at 30 days. 2) To examine the safety and tolerability of MK-383 alone and MK-383 in combination with heparin compared with heparin alone in high-risk patients with UAP/NQWMI receiving aspirin and antianginal medications, in the absence of cardiac catheterization. 3) to examine the safety and tolerability of MK-383 in combination with heparin compared with heparin alone in an invasive setting(cardiac catheterization). 4) To examine the effect of MK-383 in combination with heparin in reducing the maximal extent of angiographically-apparent thrombus compared to heparin alone.

**Technical Approach:** This multicenter, randomized, double-blind study will examine the safety and clinical efficacy of Mk-383 alone and MK-383 in combination with heparin versus heparin alone, in patients with high-risk unstable angina/non-Q-wave myocardial infarction. Patients meeting entry criteria will be randomized to receive either MK-383 alone (group A), heparin alone (group B), or MK-383 and heparin (group C). Patients will be stratified depending on whether or not they are on a continuous intravenous infusion of heparin at the time of randomization. All patients will receive conventional antianginal therapy consisting for nitrates, betablockers or calcium channel blockers, as deemed necessary by the responsible physician. During the initial 48-hour period of study drug infusion, patients will not undergo cardiac catheterization unless clinically indicated by development of refractory ischemia or new myocardial infarction. After 48 hours, all patients are expected to undergo coronary angiography (unless contraindicated) because of their high-risk clinical condition. Study drug may continue, be discontinued and resumed, or discontinued entirely depending upon the findings at time of catheterization. Study drugs may be infused for up to 96 hours (in patients who undergo PTCA/atherectomy no later than Hour 96 while on study drug, the study drug may be administered for up to a total of 108 hours after initiation). All patients will remain under close supervision until 24 hours after discontinuation of the study drug (or until clinically stable). All randomized patients will be followed for 30 days after study drug initiation and also at 6 months. Data to include vital signs, periodic laboratory evaluation, ECG and physical examination findings, adverse clinical events, refractory ischemia, new myocardial infarction, and death will be recorded on all patients. A composite goal of 1260 patients has been established. During the study period, Madigan seeks to enroll between 10 and 25 patients.

**Progress:** Four patients were randomized at MAMC to the double blind treatment. There were no adverse events. Enrollment has closed and data analysis is ongoing at the central site.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/082		<b>Status:</b> Terminated
<b>Title:</b> Aminophylline to Attenuate the Bradycardic and Hypotensive Response Observed with Transcatheter Coronary Revascularization Procedures				
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Jun 96	
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Karl C. Stajduhar, MC				
<b>Associate Investigators:</b> MAJ Patrick A. Cambier, MC			CPT Thomas M. Roe, MC	
<b>Key Words:</b> Coronary revascularization, bradycardia, hypotension				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
				<b>Periodic Review:</b> 9/30/97

**Study Objective:** The intent of this study is to determine whether the bradycardia and hypotensive response that is commonly encountered during transcatheter coronary revascularization procedures can be prevented by intravenous aminophylline administration. A secondary objective is to determine if aminophylline's attenuation of this adverse hemodynamic response dependent on the type of intervention performed (i.e. is the hemodynamic response the same for percutaneous transcatheter angioplasty (PTCA), directional coronary atherectomy (DCA), and rotational coronary atherectomy (RTCA)).

**Technical Approach:** This study will enroll selected patients undergoing one of the three types of transcatheter coronary revascularization (PTCA, RTCA, DCA). We intend to enroll 50-150 patients. Patients will have orthostatic vital signs recorded to establish that they are euvolemic prior to receiving standard pre-procedure medications. Standard cardiac catheterization procedures will be followed. After intraarterial access is obtained, baseline hemodynamic data will be recorded. Prior to the actual revascularization procedure the patient will be randomized in a double blind fashion to receive either aminophylline 5 mg/kg IV over 5-10 minutes or the equivalent volume of saline placebo. A 15 second strip of the ECG and blood pressure will be recorded just prior to initiation of the revascularization procedure and for the duration of procedure. The pre-procedure heart rate and blood pressure, and minimum heart rate and blood pressure during the procedure, will be determined. A comparison will be made between the absolute and percentage change in heart rate and blood pressure during the procedure in the treated vs. placebo group. Also reported will be the need for additional therapies to treat hypotension and bradycardia (e.g. atropine, fluid boluses, or the need for temporary pacing) in each group. The data will also be analyzed to determine if there is a difference in the hemodynamic effects by type of revascularization procedure performed in the placebo group.

**Progress:** Due to the transfer of the initial principal investigator and of two of the associate investigators, the study was terminated. No patients were entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/032		<b>Status:</b> Completed	
<b>Title:</b> Why Don't Cardiothoracic Surgeons Routinely Use Aorto-Coronary Graft Markers? A Survey of the Members of the Society of Thoracic Surgeons					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Medicine/Cardiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Allan B. Wicks, MC					
<b>Associate Investigators:</b> LTC Blaine R. Heric, MC MAJ Maureen A. Arendt, MC			CPT Kenneth M. LeClerc, MC CPT J. Olson, MC MAJ Michael D. Eisenhower, MC		
<b>Key Words:</b> Graft markers, aortocoronary, Society of Thoracic Surgeons					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To complete a survey of the members of the Society of Thoracic Surgeons, to determine: (1) the rate of Aorto-Coronary Graft Marker use among cardiothoracic surgeons, (2) reasons why some surgeons refuse to use graft markers, (3) what types of graft markers are most commonly used.

**Technical Approach:** A simple, one side-one page survey will be mailed to all members of the Society of Thoracic Surgeons (the national society in which the majority of Cardiothoracic Surgeons participate). The mailing list of approximately 5,000 members will be provided at no charge by the society, and they have expressed an interest in publishing the results, in an effort to determine if the society's practice guidelines should be amended (currently no recommendation to use, or not use, graft markers is included in published guidelines). We have already proven the dramatic beneficial impact of Aorto-Coronary Graft Markers on subsequent coronary angiography, with this data currently in press (Cathet Cardivasc Diagn, anticipate 2/97 publication). At this time, we do not expect surgeons to be aware of this data, and in fact, would like to determine their responses before this data is published. The survey will be designed in such a manner to ease data analysis (Likert scale will be used when possible) with all possible expected responses included in the survey as "choices" so as to minimize the need for "fill in the blank" responses. We will minimize the number of questions, in an attempt to maximize the number of returned surveys.

**Progress:** There were 1600 respondents to the survey. All data have been collected and the PI is currently in the process of writing a manuscript.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE  
ENDOCRINOLOGY SERVICE**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/083		<b>Status:</b> On-going	
<b>Title:</b> The Polar T3 Syndrome: Metabolic and Cognitive Manifestations, Their Hormonal Regulation and Impact Upon Performance					
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> Medicine/Endocrinology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Homer J. Lemar Jr., MC					
<b>Associate Investigators:</b> CPT Nhan V. Do, MC			COL H. Lester Reed, MC		
<b>Key Words:</b> Polar T3 Syndrome, hypothyroxinemia, thyroxine, memory, mood, muscle efficiency, energy utilization					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		04/18/97	

**Study Objective:** This is a subportion of the blanket protocol "The Polar T<sub>3</sub> Syndrome: Metabolic and Cognitive Manifestations, Their Hormonal Regulation and Impact Upon Performance". In this subportion we will: (1) Evaluate the response of central nervous system hypothyroxinemia in the development of the Polar Triiodothyronine (T<sub>3</sub>) Syndrome to thyroxine (T<sub>4</sub>) administration using the cognitive parameters of memory and mood; (2) Define the role of decreasing skeletal muscle efficiency in the increased energy requirements observed in the Polar T<sub>3</sub> Syndrome; and (3) Evaluate the effect of thyroxine supplementation on muscle efficiency and energy utilization during development of the Polar T<sub>3</sub> Syndrome.

**Technical Approach:** Sixteen military and civilian health care beneficiaries including men and women who are between 18 and 55 years old and are members of the winter-over crew in McMurdo, Antarctica will be recruited for the study. Subjects will perform monthly exercise, mood, and cognitive testing beginning one month prior to departure and continuing through their entire 11 month stay in McMurdo. The parameters that will be examined include changes in muscle oxygen utilization, changes in thyroid functions, and changes in cognitive, memory, and mood during the development of the Polar T<sub>3</sub> Syndrome. One of the characteristics of the Polar T<sub>3</sub> is a low T<sub>4</sub> state in the CNS that may be responsible for the characteristic decline in mood and memory during winter seasons in circumpolar regions. It is proposed that T<sub>4</sub> supplementation can correct the low T<sub>4</sub> state in the CNS and thus attenuate the syndrome. All subjects will be placed on placebo for the first 6 months of the study, then one-half of the subjects will be switched from placebo to levothyroxine 50 mg per day in a double blind fashion. Thyroid functions will be monitored monthly throughout the study. Subjects will serve as their own controls for analysis of mood and cognitive data. Comparisons will also be made between levothyroxine and placebo groups for the exercise, mood, and cognitive testings.

**Progress:** 16 subjects were entered during FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/146		<b>Status:</b> Completed	
<b>Title:</b> Triiodothyronine Serum Kinetics: A New Nonisotopic Method for Field and Clinical Use					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Medicine/Endocrinology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Homer J. Lemar Jr., MC					
<b>Associate Investigators:</b> CPT Nhan V. Do, MC			COL H. Lester Reed, MC LTC Marc G. Cote, MC		
<b>Key Words:</b> Triiodothyronine, kinetics, T3(non-radioactive)					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 04/18/97

**Study Objective:** This is a subportion of the umbrella protocol "The Polar T3 Syndrome: Metabolic and Cognitive Manifestations, their Hormonal Regulation and Impact Upon Performance" National Science Foundation grant #94-18466, Opp #89-22832. In this subportion we will determine if triiodothyronine (T3) kinetics studies using intravenous non-radioactively labeled T3 compare well with oral T3 and the gold standard of [125I]T3 kinetics. If this intravenous (iv) methodology closely approximates the T3 kinetic parameters obtained with isotope studies, it will provide a safe and easily usable technique to help define, manage, and better characterize the polar T3 syndrome during "field" studies carried out in the isolated regions of the Antarctic, subarctic and arctic.

**Technical Approach:** T3 kinetic parameter calculations will be performed using the iv administration of 30 mg of T3 to eight healthy male or female volunteer subjects. This technique will be validated at Madigan Army Medical Center. Both compartmental and noncompartmental analysis of the iv nonlabeled T3 disappearance will be carried out and compared with tracer 125I[T3] techniques, as well as oral nonlabeled T3 (50 mcg) administration in the same eight subjects as done in previous studies. The iv tracer studies will use 40-100 microcuries of 125I[T3], after thyroidal uptake blockade with potassium iodide using methodology we have previously reported for humans and swine. The compartmental and noncompartmental analysis of these kinetic parameters will be performed with SAAM methodology and three compartment mammillary model used as we have recently reported. The sampling times, isotope handling, hormone RIA assays, patient preparation and statistical analysis will be similar to our previous studies.

In brief, the isotope studies will be conducted for 96 hours, the IV non-labeled T3 studies for 72 h, and the oral T3 studies for 24 h with interval sampling. An exception to our earlier studies will be the sampling following nonlabeled iv T3 where blood will be obtained at 5 minutes, 15 minutes, 30 minutes and then each 30 minutes up to 10 hours as with the oral T3 studies. This study introduces the novel technique of IV T3 kinetic analysis using no radioactivity exposure. A paired comparison with other previously reported techniques by our group will provide the necessary contrast.

**Progress:** Five subjects completed the study with no adverse effects. Lab analysis is complete. The data have been sent to Dr. Rita Hays at Johns Hopkins for kinetic analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/124		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Partial Energy Restriction on the Changes in Metabolic and Kinetic Measures of Thyroid Hormone Metabolism During Antarctic Residence					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Oct 98		
<b>Department:</b> Medicine/Endocrinology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Homer J. Lemar Jr., MC					
<b>Associate Investigators:</b> CPT Nhan V. Do, MC			COL H. Lester Reed, MC Nancy S. Finney		
<b>Key Words:</b> Metabolism:thyroid hormone, antarctic residence, energy restriction, kinetic measures					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** 1) To evaluate the influence of circulating TSH and energy restriction upon the previously described increases in triiodothyronine (T3) plasma appearance rate and distribution volume (Vd) observed with extended Antarctic residence (AR). A reduction in serum TSH will be obtained by using 50mcg per day of thyroxine supplementation for the entire 11 month period, in contrast to our current study evaluating thyroxine supplement during the last 7 months of deployment. This dose schedule will allow an extension of our earlier findings regarding the effects of AR upon memory performance in this group. 2) To continue our previous mood and cognitive studies in the current study by contrasting placebo and thyroxine supplementation to insure the cognitive performance goal of supplementation has been achieved during the year as identified in our previous study.

**Technical Approach:** Sixteen military and civilian health care beneficiaries including men and women who are between 18 and 55 years old and are members of the winter-over crew in McMurdo, Antarctica will be recruited for the study. After recruitment subjects will perform monthly exercise, mood, and cognitive testing beginning one month prior to departure and continuing through their entire 11 month stay in McMurdo. The parameters that will be examined include changes in muscle oxygen utilization, changes in thyroid functions, and changes in cognitive, memory, and mood during the development of the Polar T3 Syndrome. One of the characteristics of the Polar T3 Syndrome is a low T4 state in the CNS that may be responsible for the characteristic declines in mood and memory during winter seasons in circumpolar regions. All subjects will receive either thyroxine 50mcg/day or daily placebo starting the day after October 1997 baseline studies and ending 11 months later in August 1998. Thyroid functions will be monitored monthly throughout the study. Subjects will serve as their own controls for analysis of kinetic parameters, mood and cognitive data. Comparisons will also be made between levothyroxine and placebo groups for the exercise, mood, cognitive testing, and kinetic parameters.

**Progress:** This study has not yet begun, a team of investigators leaves 1 Oct 97 to do recruitment.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,  
GASTROENTEROLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/026		<b>Status:</b> Terminated
<b>Title:</b> A Double-Blind Trial of Omeprazole versus Placebo for Prophylaxis of Sclerotherapy-Associated Esophageal Ulcer				
<b>Start Date:</b> 11/17/95		<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine/Gastroenterology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ John G. Carrougher, MC				
<b>Associate Investigators:</b>		Kris V. Kowdley, M.D.		
Michael B. Kimmey, M.D.		John Sekijima, M.D.		
Margaret Shuhart, M.D.		Lonny Hecker, M.D.		
<b>Key Words:</b> Ulcer:sclerotherapy, Omeprazole, Placebo				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** To determine whether treatment with omeprazole (Prilosec) results in prevention or more rapid healing of esophageal ulcers associated with sclerotherapy.

**Technical Approach:** Patients undergoing sclerotherapy for bleeding esophageal varices will be invited to participate. Participants will be randomized within 24 hours after the initial sclerotherapy to receive either omeprazole at a dose of 40 mg/day, or an identical placebo. The treatment period will be six weeks in duration, during which time the subjects will be monitored for the development of esophageal ulcers as seen during routine upper gastrointestinal endoscopy done for the purpose of repeat sclerotherapy. All other treatment will be continued in the normal manner. During this study, the patients will be given a brief questionnaire prior to each endoscopy to determine the presence of any symptoms associated with sclerotherapy, such as dysphagia or heartburn. Esophageal variceal sclerotherapy will be performed in the routine manner. All other testing and treatment will be performed as needed for the clinical care of the patients. Sample will be chosen to achieve an  $\alpha$  of 0.05, and a  $\beta$  of 0.1. For a difference in ulcer rate of 40% in the prophylaxis group, based on an ulcer rate of 20% in the omeprazole group and 60 in the placebo group, this would require 44 patients. Student's t-test will be used for calculating means of continuous variables, and the chi-square test or z-statistic will be used to calculate differences in complication rates among various Child's-Pugh class patients. Survival data will be analyzed using Kaplan-Meier statistics.

**Progress:** No patients were entered at MAMC. The protocol was terminated due to the departure of the principal investigator and the difficulty in enrolling patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/086	<b>Status:</b> Terminated
<b>Title:</b> The Location of the Esophageal Lesion Responsible for Dysphagia. How Accurate is the Patient's History?		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> Jan 94	
<b>Department:</b> Medicine/Gastroenterology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Roger K. Fincher, MC		
<b>Associate Investigators:</b> CPT Eric T. Fajardo, MC LTC Gregory N. Bender, MC MAJ Kazunori Yamamoto, MC		MAJ Michael F. Lyons II, MC CPT Thomas P. Peller, MC LTC Amy M. Tsuchida, MC
<b>Key Words:</b> dysphagia, esophageal lesion		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$31.65	9/30/97

**Study Objective:** To correlate the patient's localization of the site of food impaction with the site of the lesion by endoscope and barium swallow.

**Technical Approach:** The patients entered into this study will receive a directed history and physical exam as well as a CBC and thyroid function test. As part of the history, the patients will be asked to fill out a questionnaire on which foods they can swallow easily. Each food will be given a numeric value as follows: soup (1), mashed potatoes (2), peas (3), peeled apple (4), meat (5), wholemeal bread (6). A dysphagia score of 0-20 will then be established. After this initial exam the patients will receive an esophagogastroduodenoscopy (EGD) and barium swallow study per standard gastroenterology and radiology protocols. The physicians participating in the study will be blinded to the results of previous tests. The patients will be educated to the risks and benefits of the procedures and informed consent will be obtained. At the time of the procedure the patient will be asked to localize the site where food sticks or hangs up. A radiographic marker will then be placed over this/these point(s). Endoscopy and barium swallow will then be performed in the standard fashion. The site of the culprit esophageal lesion will be documented roentgenographically. We will compare the site of the lesion on the x-ray with the nipple marker. A correct localization will be defined as the nipple marker lying within two centimeters of the lesion on x-ray. Data will be analyzed descriptively by comparing the site of lesions on endoscopy and swallowing study with the external x-ray markers.

**Progress:** No further patients were entered in this study in FY 97. It has been terminated due to primary investigator staff leaving the military and no further interest in radiology to complete the study. 25 subjects had been previously entered but this number was not large enough for statistical significance.

### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol No.:** 96/164      **Status:** On-going

**Title:** Epidemiology of Gallbladder Sludge and Stones in Pregnancy

**Start Date:** 09/20/96      **Est. Completion Date:** Sep 02

**Department:** Medicine/Gastroenterology      **Facility:** MAMC

**Principal Investigator:** LTC Amy M. Tsuchida, MC

**Associate Investigators:**

MAJ Kazunori Yamamoto, MC  
LTC Byron C. Calhoun, MC  
Beth W. Alderman, M.D., MPH  
Edward J. Boyko, M.D., Ph.D.  
Katherine H. Moore, Ph.D.

Sum P. Lee, M.D., Ph.D  
LTC Roderick T. Hume Jr., MC  
Scott J. Schulte, M.D.  
Gerard Schallenberg, M.D.  
Gail Jarvik, M.D.

**Key Words:** Gallbladder, sludge, pregnancy

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost: \$0	OMA Cost: \$0.00	9/30/97

**Study Objective:** The primary objective of this NIH-funded study is to determine the incidence of gallstones and sludge during pregnancy. Other objectives are to: (1) identify behavioral and genetic risk factors for the development and regression of sludge and stones; (2) elucidate the mechanism by such risk factors may induce gallstones; and (3) predict the development and regression of sludge and stones.

**Technical Approach:** This cohort study will include serial ultrasound tests of the gallbladder during pregnancy and post-partum. All women presenting for prenatal care will be eligible unless they: (1) do not speak English; (2) have had gallbladder surgery; (3) are over 20 weeks pregnant; (4) do not expect to deliver at MAMC; and (5) are less than 18 years of age. Eligible women who agree to participate will complete Participation and Consent Forms and under waist and hip circumference measurements. The ultrasonographers will test participants for evidence of sludge and stones at 10, 18, and 28 weeks of gestation and 6 weeks postpartum. For each ultrasound test, the study radiologist will review selected ultrasound images saved by the ultrasonographer. Participants who have stones or sludge at 6 weeks postpartum will return in 12 year for a follow-up ultrasound. At her time of each ultrasound, participants will be asked to complete a one-hour questionnaire and interview. They will also be asked to give an extra fasting blood sample at 128 weeks of gestation. Medical data from the CIS and CHCS will be downloaded and linked to study data.

**Progress:** 1,044 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/093		<b>Status:</b> Completed	
<b>Title:</b> A Multicenter Randomized, Double-Blind, Evaluation of Helicobacter pylori Eradication Following Oral GR122311X in Combination with Clarithromycin Compared to Omepraole in Combination with Clarith.....					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Medicine/Gastroenterology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Amy M. Tsuchida, MC					
<b>Associate Investigators:</b> MAJ Kazunori Yamamoto, MC			LTC Robert H. Sudduth, MC MAJ John G. Carrougner, MC		
<b>Key Words:</b> <i>Helicobacter pylori</i> , <i>H. pylori</i> , clarithromycin, omeprazole					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

Study Objective: 1) To compare the following treatment groups with regard to *H. pylori* eradication rates: (a) GR122311 x 400 mg BID + clarithromycin 500 mg TID for 14 days, then GR122311 x 400 mg BID for an additional 14 days, (b) Omeprazole 40 mg QD + clarithromycin 500 mg TID for 14 days, then omeprazole 20 mg QD for an additional 14 days. 2) To compare the treatment groups with regard to duodenal ulcer healing, ulcer pain severity, antacid consumption, safety and tolerability.

Technical Approach: This is a randomized, double-blind, parallel group, double-dummy, active controlled, multicenter study. Subjects with ulcer-like pain will be tested for serum antibodies to *H. pylori* using the FlexSure™ HP serology test. Subjects with a positive test result will undergo an esophagogastroduodenoscopy (EGD), with biopsies for CLOtest®, *H. pylori* histology and culture, and antibiotic susceptibility. Subjects with a positive CLOtest® result and with endoscopic evidence of at least one duodenal ulcer will be assigned to one of two treatment groups. Subjects will be treated for 28 days. One month after treatment discontinuation, subjects will be re-endoscoped to determine duodenal ulcer healing and biopsies will be taken to determine *H. pylori* status and antibiotic susceptibility.

Progress: The study has been closed to patient entry. Four patients were randomized and completed the study. Two other patients were consented but FlexSure™ HP serology tests were negative.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/012		<b>Status:</b> On-going	
<b>Title:</b> A Pre-Clinical Research and Development Study to Evaluate Stool Specimens for Basement Membrane Fragments/Complexes and Cytoskeletal Proteins					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> Medicine/Gastroenterology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Amy M. Tsuchida, MC					
<b>Associate Investigators:</b> MAJ Kazunori Yamamoto, MC			LTC Robert H. Sudduth, MC MAJ John G. Carrougher, MC		
<b>Key Words:</b> Cancer:colon, colon tumor antigen, CoTA test strip					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** Evaluate the clinical utility potential of the CoTA test strip assay in detecting basement membrane complexes in individuals with or without colorectal cancer, respectively. And to isolate sufficient amounts of colon BMC for additional antibody production and antigen characterization using the CoTA test strip assay and other antibody tests.

**Technical Approach:** This is a multicenter trial with MAMC providing stool specimens only from patients diagnosed with colorectal cancer. Following colonoscopy, eligible participants will be instructed to collect a stool specimen after their stools have returned to normal and prior to any other intestinal procedures. The specimen will be shipped directly to BARD Diagnostic Sciences, Inc.

**Progress:** 6 subjects have been entered in FY 97.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE  
HEMOTOLOGY/ONCOLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/055	<b>Status:</b> Completed
<b>Title:</b> Agrelin (Anagrelide) for Patients With Thrombocythemia		
<b>Start Date:</b> 02/04/94	<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Timothy P. Rearden, MC	MAJ Patrick L. Gomez, MC	
LTC Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> thrombocythemia, Agrelin, safety, efficacy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	01/19/96

**Study Objective:** To assess the safety and efficacy of Anagrelide in patients suffering from thrombocythemia of various etiologies.

**Technical Approach:** Patients who are 18 years or older, free of infection and have thrombocythemia due to a myeloproliferative disorder will be asked to participate. Those consenting will have a physical examination, complete blood count and serum chemistry and then be dispensed a three-month supply of drug. During treatment with Anagrelide, blood counts should be determined as often as needed to assure patient safety. Other test will be done as clinically indicated. Any patient whose thrombocythemia is unchanged ( $\pm 20\%$ ) after two weeks of treatment will be removed from the study. Those patients receiving benefit may remain on the study until the drug is released by the FDA or all trials are terminated. The data derived from the study will be analyzed by the sponsor.

**Progress:** This drug has been approved by the FDA; therefore, this treatment study has been closed. Two patients were entered on the study; both are presently doing well.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/049		<b>Status:</b> On-going	
<b>Title:</b> An Open-Label, Long-Term, Multicenter Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough or Incident Pain in Cancer Patients Previously Enrolled in Other OTFC Studies					
<b>Start Date:</b> 01/19/96			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Medicine/Hematology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b> LTC Luke M. Stapleton, MC MAJ James S. D. Hu, MC LTC Robert L. Sheffler, MC MAJ Richard F. Williams, MC			LTC Robert B. Ellis, MC LTC Robert D. Vallion, MC MAJ John R. Caton, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Pain:cancer, fentanyl citrate					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b> 02/21/97	

**Study Objective:** To establish the long-term safety and tolerance of OTFC in cancer patients experiencing breakthrough or incident pain while taking other opioids.

**Technical Approach:** The study will be conducted using an open-label, uncontrolled design in cancer patients. Cancer patients successfully completing other appropriate studies of OTFC will be eligible for this study. When patients experience breakthrough pain, they may treat up to 4 episodes each day with OTFC. Patients will be given a supply of OTFC units, all the same dosage strength, to treat breakthrough or incident pain for one month. The patient will be contacted at least weekly by telephone by a study physician or nurse and will be seen by study personnel at least monthly. After each contact, the investigator will decide whether or not the patient requires a larger or smaller dose of study medication to relieve breakthrough pain using a single OTFC unit. Patients may remain in the study for up to four months if they continue to experience breakthrough pain and are able to provide complete and accurate information on the safety and efficacy of the study medication. Patients will record in a daily diary the use of OTFC and any other medications, assess the performance of the study medication in relieving breakthrough or incident pain, and report any adverse events they experience. Demographics, medical history, physical exam, and laboratory results will be summarized using descriptive statistics.

**Progress:** No subjects were entered FY 97, a total of 5 subjects have been entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/025		<b>Status:</b> On-going	
<b>Title:</b> Efficacy and Tolerability of 2.5 mg Itasetron Orally and of 32 mg Ondansetron Intravenously in the Prevention of Vomiting and Nausea in Patients Undergoing Cisplatin (≥75 mg/m <sup>2</sup> ) Containing.....					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b> MAJ James S. D. Hu, MC MAJ Richard F. Williams, MC			LTC Robert L. Sheffler, MC MAJ John R. Caton, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer, cisplatin, nausea, vomiting, Itasetron, Ondansetrom					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

**Study Objective:** The objectives are to evaluate the efficacy, safety, and tolerability of one-time oral administration of 2.5 mg itasetron hydrochloride and 32 mg of IV ondansetron standard therapy in the prevention of vomiting and nausea in patients undergoing high-dose cisplatin ( $\geq 75$  mg/m<sup>2</sup>) containing chemotherapy.

**Technical Approach:** This is a randomized, double-blind (double-dummy), actively controlled, multicenter, parallel-group comparison of 2.5 mg itasetron orally and 32 mg ondansetron intravenously in the prevention of vomiting and nausea. Before inclusion, potentially eligible patients will be screened -4 to 1 day before or on treatment day 1. Eligible patients will then be allocated to either of the two treatments. The medications will be given prior to initiation of cisplatin. Blinding of the treatment will be secured by using the double dummy technique. Patients will be monitored during the trial for changes in physical exam, vital signs, ECG and laboratory results. Efficacy will be measured by the frequency of complete responders (0 emetic episodes and no need for a rescue medication) within the first 24 hours after initiation of chemotherapy. Patients will be asked to maintain a diary of emetic episodes and adverse events. They will be seen for a post treatment visit 6 to 9 days after treatment.

**Progress:** No subjects were entered in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/111		<b>Status:</b> On-going	
<b>Title:</b> A Multicenter, Double-Blind, Crossover Study of Oral Transmucosal Fentanyl Citrate (OTFC) Compared to Immediate Release Morphine Sulfate for the Treatment of Breakthrough Pain in Cancer Patients ....					
<b>Start Date:</b> 06/20/97			<b>Est. Completion Date:</b> Feb 98		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b> MAJ Richard F. Williams, MC			LTC Robert L. Sheffler, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Breakthrough pain, cancer, transmucosal fentanyl citrate, morphine sulfate					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** To demonstrate that Actiq<sup>TM</sup> (oral transmucosal fentanyl citrate) is more effective for the treatment of breakthrough pain than immediate release morphine sulfate in opioid tolerant cancer patients.

**Technical Approach:** This double-blind, double-dummy, multiple cross-over, multicenter study will be conducted in cancer patients who are currently using 60-100 mg per day of oral morphine (or morphine equivalent of another oral opioid) or 50-300 µg per hour transdermal fentanyl, on around-the-clock (ATC) schedule to control persistent pain. Patients will continue to use their ATC medication for persistent pain at a constant dose and regimen throughout the study. Patients who are currently using a stable dose of 15 mg, 30 mg, 45 mg, or 60 mg capsules of immediate release morphine sulfate (MSIR) to effectively treat breakthrough (BT) pain will be eligible for the study. In the open-label titration phase (Phase A), patients will be titrated to a dose of OTFC such that one unit of OTFC will successfully treat an episode of BT pain. Successfully titrated patients will enter the double-blind phase of the study (Phase B). In Phase B, patients will be supplied with ten sequentially numbered sets of study drug - each set containing one active OTFC unit and placebo capsule(s), or one placebo OTFC unit and immediate release morphine sulfate capsule(s). The dose of MSIR that the patient used prior to study will determine the number of capsules provided. Placebo and active drug will be prepared in a way to maintain the blind. Five of the study drug sets will contain active OTFC units, and five will contain active MSIR. The order of administration of active drug will be randomized. Patients will be instructed to take IN ORDER one set of study drug (one OTFC and capsules) for each episode of BT pain they experience until all ten sets have been administered, or until they have been in the double-blind phase for 14 days. Patients will be asked to rate their pain every 15 minutes for an hour after taking the study medication. In phase B, patients will be instructed not to use additional rescue medication within one hour of treating an episode of BT pain with study drug. Patients will also be instructed not to take study drug within 2 hours of previous rescue medication. Health changes, persistent and breakthrough pain, and use of concomitant and rescue medication will be assessed daily.

**Progress:** No subjects have been entered. Have just completed initiation visit. We are screening subjects now for enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/123		<b>Status:</b> On-going	
<b>Title:</b> Efficacy and Tolerability of 2.5 mg Itasetron IV and 32 mg Ondansetron Intravenously in the Prevention of Vomiting and Nausea in Patients Undergoing Cisplan Containing Chemotherapy. A Randomized....					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b> MAJ Richard F. Williams, MC			LTC Robert L. Sheffler, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Vomiting, nausea, chemotherapy, ondansetron					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To evaluate the efficacy, safety, and tolerability of one-time IV administration of 2.5 mg itasetron hydrochloride and 32 mg of IV ondansetron standard therapy in the prevention of vomiting and nausea in patients undergoing high-dose cisplatin ( $\geq 75 \text{ mg/m}^2$ ) containing chemotherapy.

**Technical Approach:** This is a randomized, double-blind (double-dummy), actively controlled, multicenter, parallel-group comparison of 2.5 mg itasetron IV and 32 mg ondansetron IV in the prevention of vomiting and nausea. Before inclusion, potentially eligible patients will be screened -10 to 1 day before or on treatment day 1. Eligible patients will then be allocated to either of the two treatments. The medications will be given prior to initiation of cisplatin. Blinding of the treatment will be secured by using the double dummy technique. Patients will be monitored during the trial for changes in physical exam, vital signs, ECG and laboratory results. Efficacy will be measured by the frequency of complete responders (0 emetic episodes and no need for a rescue medication) within the first 24 hours after initiation of chemotherapy. Patients will be asked to maintain a diary of emetic episodes and adverse events. They will be seen for a post treatment visit 6 to 9 days after treatment.

**Progress:** No subjects have been entered since protocol was just approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/112	<b>Status:</b> On-going
<b>Title:</b> An Open-Label, Long-Term, Multicenter Study of Oral Transmucosal Fentanyl Citrate (OTFC) for the Treatment of Breakthrough or Incident Pain in Cancer Patients Previously Enrolled in AC 600 Series...		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Sep 98	
<b>Department:</b> Medicine/Hemotology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
MAJ Richard F. Williams, MC	LTC Robert L. Sheffler, MC	
MAJ Matthew P. Jones, MC	Rakesh Gaur, M.D.	
CPT Brent L. Kane, MC	MAJ William B. Reece, MC	
	MAJ Mark E. Shaves, MC	
<b>Key Words:</b> Breakthrough pain, cancer, fentanyl citrate		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To establish the long-term safety and tolerance of Oral Transmucosal Fentanyl Citrate (OTFC) in cancer patients experiencing breakthrough pain while taking other opioids and to collect data regarding patients' preferences for OTFC versus immediate release morphine sulfate.

**Technical Approach:** This open-label, multicenter study will be conducted in cancer patients previously enrolled in other AC 600 series protocols. Patients who have complete an AC 600 series protocol will be eligible for this study provided that they safely tolerate OTFC and are enrolled within four weeks of completing the earlier study. Patients will choose either OTFC or IRM (immediate release morphine) for treatment of their breakthrough pain. Patients who choose to use OTFC will start therapy at a dose selected from experience in the earlier study. Patients who choose IRM will start therapy at a dose determined from their previous rescue dose. Patients must continue to take an opioid around the clock. Medication and dosage regimen can be changed at the discretion of the investigator. Contact every two weeks between the patient and study personnel will be used as the occasion to adjust the dose of study medication up or down, as needed. Dose adjustments may be made more frequently at the discretion of the investigator. In addition, patients will be asked to maintain a diary of the study drug usage. Patients will remain in the study for up to 6 months if they continue to experience breakthrough pain and are able to provide complete and accurate information on the safety and efficacy of the study medication. Eligibility will be evaluated monthly.

**Progress:** No subjects have been entered. We are screening subjects now for enrollment.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/017	<b>Status:</b> On-going
<b>Title:</b> Evaluation of Immunity to Breast Cancer		
<b>Start Date:</b> 02/04/94	<b>Est. Completion Date:</b> Nov 94	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
LTC Robert B. Ellis, MC	MAJ Patrick L. Gomez, MC	
MAJ James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
MAJ John R. Caton, MC	MAJ Mark E. Robson, MC	
	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:breast, immunity		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$18.00	9/30/97

Study Objective: To determine the significance/relationship of CD4 helper/inducer T cell response in the presence of H2N positive/negative cancers in an attempt to determine how the immune system responds to breast cancer.

Technical Approach: Patients with breast cancer will have samples of tumor tissue obtained at the time of surgery for Her-2/neu. Blood will be obtained at the same time to evaluate for an anti-Her-2/neu T-lymphocyte response. Further venipunctures will be performed monthly during the 5 year follow-up period to continue evaluation for an anti-Her-2/neu T-lymphocyte response.

Progress: 10 subjects were entered in FY 97, for a total of 35 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/099		<b>Status:</b> Completed	
<b>Title:</b> Phase III Trial of 3-Hour versus 96-Hour Infusions of Paclitaxel from NaPro/Baker Norton in Patients with Refractory Metastatic Breast Cancer, and an Assessment of 96-Hour Infusions in 3-Hour Failures					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Nov 96		
<b>Department:</b> Medicine/Hematology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b> LTC Robert B. Ellis, MC LTC Robert D. Vallion, MC CPT Diana S. Willadsen, MC			LTC Luke M. Stapleton, MC MAJ James S. D. Hu, MC MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:breast, paclitaxel					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 06/21/96

**Study Objective:** 1) To confirm the established therapeutic effects of paclitaxel in refractory metastatic breast cancer patients given the approved dose and schedule of a new source of this novel chemotherapeutic agent. 2) To confirm the safety profile and patient tolerance characteristics of paclitaxel under the widely accepted therapeutic regimen, to offer a new regimen of paclitaxel (by 96-hour infusion) as a rescue therapy for patients progressing on the standard paclitaxel regimen, and to confirm the reported higher efficacy of the 96-hour infusion regimen of paclitaxel in a subset of patients selected randomly de novo.

**Technical Approach:** This is a multi-center, open-label, Phase II/III, trial evaluating 3-hour and 96-hour infusions of paclitaxel from NaPro/Baker Norton. The study population is women with metastatic breast cancer who have failed a maximum of two prior chemotherapy regimens, only one of which may have been as treatment for metastatic disease. The study will enroll 200 patients, approximately 75% of whom are expected to have been exposed to anthracyclines. Patients will be stratified on the basis of measurable versus evaluable disease. Patients will be randomized to the 3-hour and 96-hour infusions in each strata on a 3 to 1 ratio. Patients randomized to the treatment group using the 3-hour schedule will crossover to the 96-hour schedule when there is evidence of rapid progression. Rapid progression is defined as increase of disease within a maximum of 4 cycles of 3-hour paclitaxel infusion. Estimation of the response rate to a 3-hour infusion will be determined in 150 patients. The second objective of obtaining estimates of the response rate to a 96-hour infusion will be obtained in an additional 50 patients. The assignment of patients to infusion schedules will be done by randomization. Sample size was base on response rates of 26% and 48%.

**Progress:** This study was closed to enrollment in Jan 97. Two patients were consented and randomized at MAMC. One patient was discontinued from the trial due to disease progression and died shortly thereafter. The second patient completed the study with stable disease. She has since progressed and is receiving alternate treatment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/187	<b>Status:</b> Completed
<b>Title:</b> A Study to Evaluate the Effect of Cisplatin/Epinephrine Injectable Gel (Product MPI 5010) When Administered Intratumorally for Achievement of Treatment of Goals in Accessible Tumors of Any Histology		
<b>Start Date:</b> 09/15/95	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ John R. Caton, MC		
<b>Associate Investigators:</b>		
MAJ James S. D. Hu, MC	LTC Luke M. Stapleton, MC	
LTC Robert B. Ellis, MC	LTC Kenneth A. Bertram, MC	
MAJ Richard F. Williams, MC	LTC Robert D. Vallion, MC	
Rakesh Gaur, M.D.	LTC Robert L. Sheffler, MC	
<b>Key Words:</b> Tumors, Cisplatin, Epinephrine Injectable Gel		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To evaluate the effect of MPI 5010 on local tumor volume and local tumor volume per patient. To assess achievement of an identified primary treatment goal selected for the most troublesome tumor following up to 6 weekly treatments of MPI 5010. To observe the time to response and the time to progression for the most troublesome tumor after treatment with MPI 5010. To assess improvement and stabilization in quality of life as measured by FACT-G/H&N. To evaluate the histopathology of injected lesions that respond to local treatment with MPI 5010.

**Technical Approach:** This will be a multi-center, open label study in approximately 60-65 evaluable patients with measurable and histopathologically confirmed accessible tumors of any histology except squamous cell carcinoma of the head and neck. Prior to the enrollment, the investigator must identify the patients's most troublesome tumor and one improvable primary treatment goal for that tumor. Patients with tumors measuring at least 0.5 cm<sup>3</sup> will be treated with 0.5 mL MPI 5010/cm<sup>3</sup> of tumor volume weekly for up to 6 treatments within 8 weeks or until patient objective complete response, which ever occurs first. Patients will return for an evaluation weekly for 4 weeks after the last treatment. Patients with a 100% reduction in volume of all treated tumors at the end of the Treatment Phase will be followed monthly for an additional 5 months or until time of tumor progression. Re-treatment of a tumor in follow-up in the case of disease or symptom progression may be performed if, in the opinion of the investigator, it will benefit the patient. Data analysis will include progress toward treatment goal, quality of life, tumor response, dosing, and safety. Appropriate statistical tools will be employed to measure and test each parameter in support of the objectives.

**Progress:** Enrollment in this study was discontinued in Feb 97 due to the departure of the principal investigator. Two patients were randomized at MAMC. Treatment of the first participant was stopped due to a lack of efficacy as determined by the investigator. The second participant elected to withdraw from the study due to an a bleeding duodenal ulcer and fear of tumor ulceration with continued treatment. Both the PI and the gastroenterologist stated that the ulcer was attributed to Motrin and not related to the study medication.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/133		<b>Status:</b> Completed	
<b>Title:</b> A Double-Blind, Randomized, Phase 3, Multicenter Study of Suramin and Hydrocortisone vs Hydrocortisone and Placebo in the Treatment of Patients with Metastatic, Hormone-Refractory Prostate Carcinoma					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b> LTC Kenneth A. Bertram, MC LTC Luke M. Stapleton, MC MAJ J. Brantley Thrasher, MC			LTC Robert D. Vallion, MC LTC Robert B. Ellis, MC James H. Timmons, MD		
<b>Key Words:</b> Cancer:prostate, Suramin, Hydrocortisone					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					05/17/96

**Study Objective:** To determine suramin's effect on pain, performance status, PSA, disease response, quality of life and survival in patients with hormone-refractory prostate carcinoma. Also to evaluate the safety of suramin.

**Technical Approach:** This study will be a double-blind, randomized, placebo-controlled, multi-center study of suramin plus hydrocortisone therapy versus placebo plus hydrocortisone therapy in 20 MAMC patients (total of 186 per treatment group) with prostatic carcinoma who have failed at least 1 course of prior hormonal manipulation. The primary outcome measurements will include changes in PSA level, disease response, quality of life, survival, time to progression, time to response and duration of responses. Patients will be stratified prospectively on the basis of PSA levels and presence of measurable disease and then randomly assigned to the suramin or placebo treatment groups. Patients will be given fixed doses of suramin or placebo, infused intravenously over a 1-hour period over a 78-day treatment period. Both arms will receive concomitant hydrocortisone. Primary efficacy determination will be determined on the basis of changes relative to baseline in pain score, analgesic use and performance status. Secondary efficacy measurements will be made on the basis of changes relative to baseline in other BPI scales, PSA changes, measurable disease response, and quality of life. Descriptive statistics will be provided for all demographic, efficacy and safety parameters. All tests will be 2-sided and conducted at the 5% level of significance. The level of significance will not be adjusted for the planned comparisons. Appropriate statistical methods will be applied to the various parameters and will include analysis of covariance, Cochran-Mantel-Haenszel analysis, and the Wilcoxon test.

**Progress:** This study was closed to patient enrollment in Jun 97 due to sufficient patient accrual. Two patients were entered with no adverse events.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/138		<b>Status:</b> On-going	
<b>Title:</b> Phase 2/3 Placebo Controlled Trial of Targretin Capsules (LGD1069) in Patients with Advanced Non-Small Cell Lung Cancer					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Matthew P. Jones, MC					
<b>Associate Investigators:</b> LTC Robert L. Sheffler, MC LTC Kenneth A. Bertram, MC			MAJ Richard F. Williams, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:lung, targretin, efficacy, safety, tolerability					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

**Study Objective:** 1) To determine whether Targretin capsules administration at a high (600 mg/m<sup>2</sup>/day) or a moderate dose (300 mg/m<sup>2</sup>/day) is more effective than placebo in prolonging-free interval (survival) in patients with Stage IIIB with pleural effusion, Stage IV, or recurrent, non-small cell lung cancer who have previously been stable or had tumor regression following platinum-based combination chemotherapy; 2) to evaluate the safety and tolerability of Targretin capsules when administered to non-small cell lung cancer patients following platinum-based combination chemotherapy; and 3) to document objective antitumor responses to Targretin capsules that occur in patients with measurable or evaluable non-small cell lung cancer at study entry.

**Technical Approach:** This is a multicenter, Phase 2/3, double-blinded, randomized, placebo-controlled trial comparing two dosing levels of Targretin capsules to placebo with regards to progression free-survival in patients with Stage IIIB, Stage IV, or recurrent non-small cell lung cancer who are stable or responding to platinum-based combination chemotherapy. Patient and Investigator will be blinded to the drug assignment and will be unblinded to the dose level assignment. Eligible patients who have signed the consent form will be randomized to one of the following three arms: 1) Arm I: Targretin capsules at 600 mg/m<sup>2</sup>/day as a single daily dose; 2) Arm II: Targretin capsules at 300 mg/m<sup>2</sup>/day as a single daily dose; and 3) Arm III: Placebo capsules either 600 mg/m<sup>2</sup> day (Arm IIIA) or 300 mg/m<sup>2</sup>/day (Arm IIIB) as a single daily dose. Therapy will continue until disease progression, patient withdraw, dose-limiting toxicity or death. Date and cause of death will be obtained on all patients. Patients will be evaluated for tumor assessment at baseline, every eight weeks during treatment, and at study termination. Patients who progress while receiving Targretin capsules or placebo will be removed from the study. The primary efficacy endpoint of the study is the progression-free interval (survival) (time from study entry to progressive disease). The secondary efficacy endpoint is overall survival (time from study entry until death). Additional efficacy parameters evaluated will include quality of life measures according to the Lung Cancer Symptom Scale.

**Progress:** Study is awaiting CIRO approval to start.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/170	<b>Status:</b> Completed
<b>Title:</b> Phase 3 Trial of Gemcitabine Plus Cisplatin Versus Cisplatin Alone in Patients with Metastatic Non-Small Cell Lung Cancer		
<b>Start Date:</b> 07/21/95	<b>Est. Completion Date:</b> Sep 96	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC		
<b>Associate Investigators:</b> MAJ James S. D. Hu, MC LTC Robert B. Ellis, MC MAJ John R. Caton, MC Rakesh Gaur, M.D.	LTC Kenneth A. Bertram, MC LTC Robert D. Vallion, MC LTC Luke M. Stapleton, MC LTC Robert L. Sheffler, MC	
<b>Key Words:</b> Cancer:non-small cell lung, gemcitabine, cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** The primary objective of this study is to compare the survival of patients with Stage III and IV metastatic NSCLC treated with cisplatin alone to that of patients treated with the combination of cisplatin and gemcitabine.

**Technical Approach:** This is a randomized study of cisplatin monotherapy versus the combination of cisplatin and gemcitabine in patients with locally advanced (unresectable Stage IIIA or IIIB), or metastatic NSCLC who have received no prior chemotherapy regimens. Approximately 520 patients will be enrolled in this study and be randomized to receive either Regimen A or Regimen B. Regimen A is defined as follows: gemcitabine will be administered intravenously once each week for 3 weeks, followed by a 1-week rest period, and cisplatin will be administered intravenously once each cycle immediately after the first gemcitabine infusion of that cycle. This 4-week schedule defines a cycle of treatment. Multiple cycles will be administered. Regimen B is defined as follows: cisplatin will be administered intravenously once each cycle. Patients may receive a maximum of 6 cycles. It is anticipated that 10 to 15 patients will participate at Madigan.

**Progress:** This study was closed to enrollment 25 Feb 97. Three patients were randomized at MAMC. One patient completed the trial with stable disease but has since progressed and initiated alternate therapy. One patient had rapid progression after cycle 2, was taken off study, and started on alternate treatment. He has since died from disease progression. One patient had a good response after cycle 2, followed by no change after cycle 4. He elected to discontinue study due to side effects. He continues to have stable disease.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/138		<b>Status:</b> On-going	
<b>Title:</b> The Effect of Tamoxifen and Ionizing Radiation on Expression of Bcl-2, Bcl-x, and p53 in Breast Cancer Cells In Vitro					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC					
<b>Associate Investigators:</b> MAJ Nyun C. Han, MC Katherine H. Moore, Ph.D.			LTC Robert B. Ellis, MC MAJ Mark D. Brissette, MC		
<b>Key Words:</b> Cancer:breast, oncogenes, tamoxifen, radiation					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The objective of this study is to define the molecular mechanism by which antitumor agents such as estrogen receptor antagonists and ionizing radiation initiate programmed cell death (apoptosis) in cultured breast cancer cells. Specific objectives are to examine the treated breast cancer culture cells for morphologic and biochemical evidence of apoptosis and to determine the time course for apoptotic death as well as that for changes in the level of bcl2 and p53 in the cells. Thereby, we will determine if changes in the level of these factors precede the onset of apoptotic death and provide evidence for the importance of modulation of the expression of these proteins as antitumor effects of these agents. Also, changes in other bcl2-related factors such as bax and bcl-x will be examined.

**Technical Approach:** Three breast cancer cell lines will be used MCF-7, MDA-MB-231, and ZR-75. Cells from each of these lines will be grown in the presence of estrogen for 24 hours, after which the medium will be treated with either tamoxifen or 4-hydroxytamoxifen, at 0.1 and 1.0 micromolar for six days. For the effects of radiation, cell will be grown in estrogen for 24 hours and then irradiated. At 24 hour intervals, cells from each experimental condition will be harvested and examine for apoptosis and for the level of expression of bcl2, bcl-x and p53. Morphologic and biochemical evidence for apoptosis in these cultures will be obtained by light microscopy and DNA agarose gel electrophoresis. Flow cytometry will be used to determine the fraction of apoptotic cells. Expression of the protein products of the three oncogenes will be determined by quantitative Western blot electrophoresis. The mean and standard deviations for three separate cultures with each treatment at each time point will be determined. Statistical analysis will be performed using two way analysis of variance methods.

**Progress:** We found that tamoxifen produces a dose-related increase in the apoptotic rate in the ER positive cell line (MCF-7) at doses ranging from  $10^{-7}$  to  $5 \times 10^{-6}$  M. Tamoxifen also produced an increase in apoptosis of the ER negative cell line (MDA-MB-231) but only at the highest doses ( $10^{-5}$  M). Correlating with the effect of tamoxifen on apoptosis, we found a decrease in the expression of BCL-2 protein with increasing tamoxifen dose. Therefore it appears that tamoxifen increases the rate of apoptosis in ER positive breast cancer cells and that this effect may be mediated through a decrease in the level of expression of the apoptotic inhibitory factor BCL-2. Whether this represents a direct effect on BCL-2 gene regulation or an indirect effect through an estrogen receptor-mediated pathway is unknown. The effect was noted in an ER negative cell line, but only at much higher doses. Interestingly, megestrol acetate has no effect on apoptosis in either cell line.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/162		<b>Status:</b> On-going	
<b>Title:</b> The Characterization of Breast Cancer Susceptibility Genes in Males and Their Kindred					
<b>Start Date:</b> 08/18/95			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC					
<b>Associate Investigators:</b> Amelia Langston, M.D. MAJ John R. Caton, MC			LTC Robert B. Ellis, MC Elaine Ostrander, Ph.D.		
<b>Key Words:</b> Cancer:breast, genes:BRCA1, BRCA2, AT, p53, RB, ras					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** Using male breast cancer patients as probands we will characterize the known breast cancer susceptibility genes BRCA1, BRCA2, AT and additional genes such as p53, RB and ras in the affected individuals and their families.

**Technical Approach:** The data obtained from a previous study of the Automated Central Tumor Registry database (ACTUR) revealed 123 total cases of male breast cancer within the Department of Defense (DOD) healthcare system. Those patients with a family history of breast cancer are currently in the process of evaluation under a previous IRB approved protocol. The next step involves collecting samples of blood from each living male breast cancer patient and family members of both living and deceased patients as deemed appropriate for study. Additionally, formalin fixed paraffin imbedded tumor blocks will be collected on as many patients as possible. Once the specimens are collected the blood will be processed at Madigan Army Medical Center. Both DNA and buffy coat cells will be extracted and frozen for storage. Aliquots of these specimens along with portions of tumor blocks will be blinded with regard to clinical information and sent to Dr. Ostrander's lab at Fred Hutchinson Cancer Research Center for analysis. This analysis will initially include screening for mutations in BRCA1, BRCA2 (when cloned) and the Ataxia-Telangiectasia gene (AT) using the patient DNA extracted from the blood sample. The tumor blocks would be tested for the loss of heterozygosity for markers on chromosomes 13q covering both the BRCA2 and Retinoblastoma (RB) genes, chromosome 11 for the AT gene and chromosome 17 regions covering the p53 and BRCA1 genes. Data collected from these studies would then be matched with the clinical information in order to derive information regarding cancer susceptibility, prognosis and basic mechanisms of carcinogenesis.

**Progress:** A total of 25 has been entered and blood samples are undergoing genetic analysis. This is approximately 50% of the patients needed. Enrollment will continue. The principal investigator was changed from Dr. John Caton to Dr. Williams in June 1997.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/118		<b>Status:</b> Completed	
<b>Title:</b> Phase II Study of Single Agent Thiotepa for Advanced, Hormone-Refractory Prostate Carcinoma					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC					
<b>Associate Investigators:</b> MAJ J. Brantley Thrasher, MC MAJ Richard C. Tenglin, MC			Celestia S. Higano, MD MAJ Timothy P. Rearden, MC LTC Robert B. Ellis, MC		
<b>Key Words:</b> Cancer:prostate, thiotepa					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** The purpose of this study is to evaluate the efficacy and toxicities of single agent thiotepa for advanced hormone-refractory prostate carcinoma.

**Technical Approach:** This is a non-randomized phase II study. All eligible patients with metastatic, hormone-refractory prostate cancer who are considered by their physicians to have a chance to benefit and also agree to participate will be entered. Patients will be initially staged with abdominal/pelvic C.T. scans, bone scans, chest radiographs, serum PSA, serum PAP, BUN, creatinine, liver function tests and complete blood count. All patients will receive thiotepa 50 mg/m<sup>2</sup> by intravenous administration at 28 - day intervals. Patients will be continued on therapy until: 1) disease progression is documented; 2) Unacceptable toxicities occur; or 3) the patient refuses further treatment for any reason. Any patient obtaining a complete response will receive two (2) additional courses of thiotepa past CR, and then be followed off therapy.

**Progress:** Three patients were entered on this study in previous years and all have died of disease.

PI was changed from Dr. Robert Ellis to Dr. Williams.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/026	<b>Status:</b> On-going
<b>Title:</b> A Phase II Trial of Thioplex Following Induction Chemotherapy to Decrease the Incidence of Brain Metastases in Limited Stage Small Cell Lung Cancer Patients		
<b>Start Date:</b> 11/15/96	<b>Est. Completion Date:</b> Jan 98	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
MAJ James S. D. Hu, MC	LTC Robert B. Ellis, MC	
Rakesh Gaur, M.D.	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:lung, small cell, Thioplex, brain metastases		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/21/97

**Study Objective:** The primary objective is to evaluate the effectiveness of Thioplex in the prevention of CNS metastases in limited stage SCLC subjects who have achieved a complete or partial remission following initial systemic chemotherapy and chest irradiation. Secondary objectives are to evaluate the treatment with respect to overall survival, incidence of systemic metastases, and safety.

**Technical Approach:** This is a multicenter, open label, Phase II pilot study designed to evaluate the efficacy of Thioplex following a standard Etoposide (VP-16)/platinum-based regimen for the prevention of CNS metastases in limited small cell lung cancer. Patients who have achieved a complete or partial remission following chest irradiation and four courses of standard induction chemotherapy will be eligible for the study. Subjects will receive Thioplex at a dose of 45 mg/m<sup>2</sup> IV each month for 3 cycles. Patients will be followed for up to 30 months for evidence of CNS metastases and survival.

**Progress:** No subjects have been entered in FY 97. No one has met the criteria for the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/040		<b>Status:</b> Terminated	
<b>Title:</b> Multicenter, Open-Label, Randomized, 2-Arm, Phase II Trial of Letrozole (2.5 mg p.o. q.d.) versus the Combination of Letrozole (2.5 mg p.o. q.d.) + Tamoxifen (20.0 mg p.o. q.d.) As First-Line ...					
<b>Start Date:</b> 12/19/96			<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Medicine/Hemotology-Oncology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC					
<b>Associate Investigators:</b> LTC Kenneth A. Bertram, MC MAJ James S. D. Hu, MC Rakesh Gaur, M.D.			LTC Robert L. Sheffler, MC LTC Robert B. Ellis, MC MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:breast, letroole, tamoxifen					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** 1) To determine the efficacy of the two treatment arms, specifically: objective tumor response rate, time to tumor progression and time to treatment failure. 2) To determine the safety and tolerability of the two treatment arms. Secondary objectives: To determine survival times for each treatment arm.

**Technical Approach:** This is a multicenter, open label, randomized 2-arm, Phase II trial of letrozole (2.5 mg po qd) versus the combination of letrozole (2.5 mg po qd) + tamoxifen (20 mg po qd) as first line treatment in post menopausal women with advanced breast cancer. Clinical safety evaluations will be performed at baseline (prior to trial treatment), after 1 month, 3 months, and every 3 months thereafter until the patient is discontinued from the trial. Tumor evaluations will be performed at baseline (prior to trial treatment) and every 3 months thereafter, or at any other time signs or symptoms suggest suspected cancer progression. Any patient who manifests an objective tumor response (complete or partial response) will have a full tumor evaluation repeated at least 4 weeks later, but not more than 3 months (the next scheduled tumor assessment visit) after the initial observation of tumor response to confirm the presence of the response.

**Progress:** This study was terminated in Mar 97 by the sponsor due to initial pharmacokinetic data which showed that serum levels of letrozole were reduced by approximately 31% when used in combination with tamoxifen. No patients were enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/110	<b>Status:</b> On-going
<b>Title:</b> Double Blind, Double Dummy, Randomized, Multicenter, 2-Arm, Phase III Trial Comparing Letrozole 2.5 mg versus Tamoxifen 20 mg as First Line Therapy in Postmenopausal Women with Advanced Breast Cancer		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Aug 01	
<b>Department:</b> Medicine/Hematology-Oncology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC		
<b>Associate Investigators:</b> LTC Kenneth A. Bertram, MC James H. Timmons, MD		
LTC Robert L. Sheffler, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:breast, letrozole, tamoxifen, postmenopausal		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To compare the efficacy, as evaluated by the primary variable of time to progression (TTP), and the secondary variables of objective response rate, duration of response, and time to treatment failure (TTF) between the two treatment arms (2.5 mg letrozole once daily and 20 mg tamoxifen once daily). Secondary: a) To compare the tolerability and toxicity of the two treatment arms; b) to determine the survival time in each of the two treatment arms; and c) to summarize time to progression, objective response rate, and time to treatment failure for the second-line therapy using the subset of patients in the cross-over treatment period.

**Technical Approach:** This is a double blind, double dummy, multicenter, randomized, 2-arm, cross-over, Phase III trial, comparing the efficacy of letrozole versus tamoxifen in first-line treatment of postmenopausal women with advanced breast cancer. Once patients have met the inclusion/exclusion criteria, they will be randomly assigned to one of the two treatment arms. The two treatments are randomly assigned according to a predetermined, computer generated randomization list using permuted blocks. Patients will be evaluated radiographically every three months for disease progression. If they remain disease free, they will be seen for an exam, laboratory tests and re-dispensing of blinded trial medication. Once disease progression has been documented, patients will be given the option of taking open label letrozole (if they were on prior treatment with tamoxifen) or open label tamoxifen (if they were on prior treatment with letrozole) and will continue to be followed every three months.

**Progress:** Study has not yet started, awaiting contract approval.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,  
INFECTIOUS DISEASE SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/132		<b>Status:</b> Completed
<b>Title:</b> An Open-Label, Multicenter Study of Clinafloxacin in the Treatment of Infective Endocarditis				
<b>Start Date:</b> 05/19/95		<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Medicine/Infectious Disease		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Ronald H. Cooper, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Endocarditis, Clinafloxacin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		05/17/96

**Study Objective:** To assess the efficacy of clinafloxacin in the treatment of patients with infective endocarditis.

**Technical Approach:** This study will evaluate the safety and efficacy of clinafloxacin in 50 patients (5 to 10 from MAMC) with infective endocarditis of bacterial etiology for survival rate, time to defervescence, time to sterile blood cultures and development of resistant pathogens. The dosage will be clinafloxacin 200 mg intravenously or by mouth every 12 hours for 4 to 6 weeks, up to 12 weeks maximum. The primary efficacy parameter is the microbiological eradication rate. Patients will be stratified on the basis of (1) right-sided vs left-sided endocarditis, (2) native valve versus prosthetic valve infection, and (3) pathogen recovered from blood cultured.

**Progress:** No eligible patients consented to enter this study at MAMC, and the principal investigator elected to close the study after a two year screening period.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,  
INTERNAL MEDICINE SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/008	<b>Status:</b> Terminated
<b>Title:</b> Are Sputum Cultures Useful in the Management of Uncomplicated Community-acquired Pneumonia		
<b>Start Date:</b> 10/18/96	<b>Est. Completion Date:</b> Apr 97	
<b>Department:</b> Medicine/Internal Medicine <b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Roger K. Fincher, MC		
<b>Associate Investigators:</b> LT Joan Morris, NC USN		
<b>Key Words:</b> Pneumonia, sputum		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To see if sputum cultures affect antibiotic choices in the setting of community-acquired pneumonia (CAP).

**Technical Approach:** Retrospective Arm, review of 100 patients admitted to the Internal Medicine and Family Practice inpatient services using CIS, CHCS, completed inpatient records, and outpatient records. Sputum gram stains, sputum cultures, antibiotic choices and changes, and clinical outcome will be compared and analyzed.

Prospective Arm, random assignment of uncomplicated CAP patients meeting inclusion and exclusion criteria from APCC, FP Clinic, Emergency Department, and inpatient services to two groups. One group will have sputum cultures attained and one group will not have sputum cultures. Sputum gram stains will be attained on all patients. Management of patients will be at discretion of staff and resident physicians caring for individual patients based on standard of care patterns as recommended by the American Thoracic Society. Any changes in antibiotic will be documented. Gram stain results, culture results, antibiotic choices and changes, and clinical outcome will be compared and analyzed.

**Progress:** The IRB required extensive revisions to this protocol. The PI was unable to make required revisions and complete the protocol in the time that he left at MAMC. Therefore, he terminated it.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/049		<b>Status:</b> Completed	
<b>Title:</b> Are Hemoglobins and Potassiums Drawn From Intravenous Heparin Locks Accurate?					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Medicine/Internal Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Roger K. Fincher, MC					
<b>Associate Investigators:</b>			CPT Jeffrey S. Strong, MC		
<b>Key Words:</b> Hemoglobin, potassium, heparin locks					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To see if hemoglobin and potassium measurements drawn from heparin-lock peripheral catheter lines in routine clinical situations correlate to the directly drawn hemoglobin and potassium.

**Technical Approach:** After assuring inclusion and exclusion criteria are met and informed consent obtained, 30 patients will have IV heparin-lock sampling and subsequent direct venous sampling sent for hemoglobin and potassium determination. The results will be recorded and the data analyzed using Limits of Agreement analysis.

**Progress:** Catheter sampling was attempted on 53 patients. Of these, 32 successfully had a peripheral venous catheter sample drawn. A 42% success rate was seen with 20 gauge catheters and a 78% success rate with 18 gauge catheters. Potassium values obtained by peripheral catheter and venipuncture sampling showed poor correlation via limits of agreement analysis. Thus, the use of peripheral catheter sampling was unacceptably inaccurate for clinical use. Hemoglobin values showed a good correlation with both linear regression and limits of agreement analysis. Sub-group analysis of patients either getting no IV infusions or intermittent infusions showed acceptable correlation of hemoglobin measurements between the two techniques, but unacceptable potassium correlation. The success rate of catheter sampling is dependent on catheter size, with larger gauge catheter being more successful.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/113	<b>Status:</b> On-going
<b>Title:</b> Optimal Bowel Preparation for Flexible Sigmoidoscopy: Oral Magnesium Citrate with Oral Bisacodyl or with Two Hypertonic Phosphate Enemas		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Mar 98	
<b>Department:</b> Medicine/Internal Medicine <b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Roger K. Fincher, MC		
<b>Associate Investigators:</b>		
MAJ Jeffrey L. Jackson, MC	CPT Jeffrey S. Strong, MC	
LTC Amy M. Tsuchida, MC	CPT Jon D. Roebuck, MC	
Laurie Harrell	LTC Robert H. Sudduth, MC	
<b>Key Words:</b> Sigmoidoscopy, bowel preparation, magnesium citrate, Fleet enema		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	9/30/97

Study Objective: To study the differences between a single or double enema preparation, combined with magnesium citrate orally versus oral bisacodyl combined with oral magnesium citrate use.

Technical Approach: This study will compare three bowel preparation regimens: a) 296 ml of magnesium citrate taken orally the night prior to the procedure, followed by 2 hyperphosphate enemas, taken 1 and 2 hours before the procedure, respectively, b) 296 ml of magnesium citrate taken orally the night prior to the procedure followed by a single hyperphosphate enema taken 1 hour before the procedure, and c) 296 ml of magnesium citrate taken orally the night prior to the procedure, immediately followed by 20 mg of dulcolax, also taken orally.

Progress: 58 subjects were entered during FY 97, for a total of 67 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/016		<b>Status:</b> On-going	
<b>Title:</b> A Controlled Clinical Trial to Improve Housestaff Identification of and Attitudes Toward Mental Disorders in Primary Care					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> Medicine/Internal Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Robert V. Gibbons, MC					
<b>Associate Investigators:</b> MAJ Richard A. Jordan, MC			CPT Jeffrey S. Strong, MC MAJ Jeffrey L. Jackson, MC		
<b>Key Words:</b> Mental Disorders, identification, attitudes					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

Study Objective: To determine whether simple educational intervention can increase the rate of recognition of mental disorders.

Technical Approach: As at least one third of all patients seen in an outpatient setting by primary care physicians have an underlying mental disorder, and the rate of identification of such problems by this group of physicians is generally under 50%, this educational intervention will attempt to improve housestaff attitudes toward recognition and management of psychiatric disorders.

Progress: 11 subjects have been piloted, and has recently switched PIs.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/156	<b>Status:</b> Completed
<b>Title:</b> A Pilot Study of the Semmes-Weinstein Monofilament for Diagnosing Peripheral Neuropathy in Diabetics: Inter-rater Reproducibility and Comparison with Standard Clinical Examination		
<b>Start Date:</b> 09/20/96	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Medicine/Internal Medicine <b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jeffrey L. Jackson, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Diabetes, Semmes-Weinstein monofilament, neuropathy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To assess the inter-rater reproducibility and to compare the Semmes-Weinstein monofilament in the detection of peripheral neuropathy in diabetics.

**Technical Approach:** Loss of foot sensation is a common complication of diabetes mellitus and may lead to ulceration, infections, and amputation. A simple device consisting of a monofilament mounted on a plastic stick has been developed to enable the clinician to detect protective sensation in the foot. In this pilot study, we will examine basic measurement properties of this device: how reproducible are the results of foot examination by two examiners, using the monofilament and standard physical examination? The study will consist of two five-minute examinations by two physicians of each subject's feet during a single clinic visit for each subject. This will be a pilot study for a possible future multi-center physical examination study by the U.S.-Canadian Research Group on the Clinical Examination.

**Progress:** Thirty patients were entered at MAMC in this multicenter trial. Data are being analyzed centrally.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/161		<b>Status:</b> Completed	
<b>Title:</b> The Relationship Between Intensity of Anticoagulation and Complications					
<b>Start Date:</b> 09/20/96			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Medicine/Internal Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jeffrey L. Jackson, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Anticoagulation, coumarin, thrombosis					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To measure the relationship between the intensity of anticoagulation with coumadin and potential bleeding and thrombotic complications.

**Technical Approach:** The coumadin data base at MAMC is an automated system for following patients taking coumadin. The system changed methods of tracking degree of anticoagulation in 1993 to the International Normalized Ratio (INR). There are approximately 800 patients in this data set which have been followed for up to three years. Data elements present within this data set include patient demographics, indication for initiation of coumadin, the target INR, the actual recorded INR values, the doses of coumadin given and, for patients withdrawn from coumadin, the indication for withdrawal. I propose to extract these data elements and analyze the INR values with respect to the optimal INR. Generally speaking the two significant outcomes of interest are cerebral vascular accidents, generally indicative of inadequate coumadinization and bleeding complications from overzealous treatment. The hope is to define an optimal INR to minimize both complications. Combined databases of MAMC and WRAMC total 2300 total patients which will be retrospectively analyzed. The total number of patient-years will be subdivided by INR intervals of 0.5. For each patient, the fluctuation of INR around the target value is measured at regular intervals. We will assume that the INR changes in a linear fashion between measurements and will allocate a specific INR accordingly, to each day. Days will then be grouped according to INR intervals and summed for all patients--this will generate patient-years at different intensities. If there is greater than 8 weeks between two measurements, no INR will be allocated, since this duration may make the linear assumption invalid. The ratio of the number of events that took place when the prothrombin time is in a particular INR range to the number of patient-years during which the INR is at this level in the patient population will be the fundamental unit of analysis. 95% confidence intervals for the incidence rates will be calculated with the assumption of Poisson distribution. Logistic regression analysis using demographic and INR data to model predicted likelihood of a complication. Cox proportional hazard model will be used to assess the likelihood of failure using both demographic and INR data.

**Progress:** 5,867 patient records were downloaded from the automated coumadin database in the MAMC Cardiology Clinic in this multicenter study. Exploratory data analysis was performed. A cross-search among RCMAS database for these patients searching for potential complications found none. Downloading of similar data is in progress at TAMC and WRMAC. The principal investigator, who has been reassigned to WRAMC, will synthesize data and produce results at WRAMC in next 6-9 months.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/155		<b>Status:</b> Completed
<b>Title:</b> Symptom Related Expectations in A Rheumatology Clinic Setting				
<b>Start Date:</b> 09/20/96		<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jeffrey L. Jackson, MC				
<b>Associate Investigators:</b>		MAJ Edmund H Hornstein, MC		
<b>Key Words:</b> Rheumatology, symptoms				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** a) To determine the prevalence of mood, anxiety and somatoform disorders in patients making an initial visit to a rheumatology subspecialty clinic; b) to determine whether a relationship exists between mental disorders and the likelihood of objective abnormal findings on physical examination or laboratory; and c) to determine whether a relationship exists between mental disorders and the likelihood of organic rheumatologic diagnosis.

**Technical Approach:** 75 patients presenting with a new consult to the rheumatology clinic will be asked to participate. After obtaining verbal consent, patients will fill out a questionnaire on symptom-related expectations as well as the PRIME-MD screen. After the visit, rheumatologists will complete a one-page questionnaire on their clinical assessment. The data will be encoded into a database using the EPI-INFO system developed by the CDC for epidemiological studies. Simple descriptive analysis, such as frequency of various psychiatric disorders, mean ages, frequency of specific rheumatologic diagnosis, will be performed. The chi-square statistic can also be performed to analyze the relationship between the presence or absence of a psychiatric disorder and the presence of organic pathology. Predictors of likelihood of having either a disorder or objective findings will be performed using logistic regression techniques using STATA statistical packages. We previously found that patients undergoing EGD without a psychiatric disorder had abnormalities present 45% of the time, compared to 15% in patients with a psychiatric disorder. Assuming that this 30% difference also holds in rheumatologic patients and further assuming a 50% prevalence of psychiatric disorders, sample size calculations (assuming  $\alpha=0.05$ ,  $\beta=0.20$ ,  $H_0: 0.45\%$ ,  $H_1: 0.15\%$ ) would be 35 patients, requiring a total of 70 patients.

**Progress:** Sixty-three patients were enrolled at MAMC and 150 at WRAMC in this multicenter study. Data have been entered in a database and analysis is in progress at WRAMC. It appears from preliminary analysis that the incidence of symptom-related expectations and psychiatric disorders is the same as in the general medicine clinic. More patients will be entered at WRAMC. The principal investigator has been reassigned to WRAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/048		<b>Status:</b> Terminated	
<b>Title:</b> The Effect of Left Ventricular Hypertrophy on Diastolic Function at Rest and After Exercise					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Medicine/Internal Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kenneth M. LeClerc, MC					
<b>Associate Investigators:</b> CPT Stephen J. Fleet, MC			MAJ Patrick A. Cambier, MC CPT Eric M. Osgard, MC		
<b>Key Words:</b> Hypertrophy, diastolic function, exercise, rest					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To evaluate dastolic function in two populations with left ventricular hypertrophy (LVT) at rest, after acute exercise testing, and following aerobic exercise training.

**Technical Approach:** A predetermined number (15-50 per group) of younger subjects (<45 years of age) with either isolated pathologic LVH (i.e. attributed to a primary medical problem) or physiologic LVH (attributable to exercise training) will undergo elective echocardiographic evaluation at rest and immediately after maximal exercise testing. Measures of diastolic function will be compared between these two groups. In addition, both groups will electively undergo a prescribed aerobic exercise program for 10 weeks and the effect on dastolic function will be re-assessed echocardiographically and differences within and between groups will be described. The echocardiographic studies will be analyzed by blinded observers for assessment of diastolic function using existing computerized analysis and compared using paired and unpaired T-tests.

**Progress:** This study was terminated due to difficulty recruiting an adequate number of subjects and a change in priorities for the training and research of the principal investigator. No statistical differences were noted based on the data of a limited number of subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/091		<b>Status:</b> Terminated
<b>Title:</b> Can Antibody Response to Pneumococcal Vaccination Be Enhanced by Pretreatment with Vitamin B12				
<b>Start Date:</b> 04/19/96		<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Emil P. Lesho, MC				
<b>Associate Investigators:</b>		COL Ronald H. Cooper, MC		
<b>Key Words:</b> Penumococcus, vaccination, vitamin B12				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** To determine if prior treatment with cobalamin enhances immunogenic response to pneumococcal vaccination in immunocompetent patients.

**Technical Approach:** Patients who are determined to require pneumococcal vaccination as part of routine health maintenance will be asked if they wish to participate in a study to see if the effectiveness of the vaccination can be enhanced with vitamin B12. If so, informed consent will be obtained, and at least 40 patients will be randomized into 2 groups of 20 patients each. Overall nutritional, immunologic, vitamin B12 status will be assessed. One group will receive hydroxocobalamin injection, the other will receive sterile saline as the placebo. One to two weeks later, the patients will then have cobalamin levels reassessed to see if replacement was successful. Those in the treatment group will be given another dose of B12 along with their routine pneumococcal immunization. Those in the control group will be given the placebo along with the pneumococcal vaccine. One to two months after this, patients will then have quantitative pneumococcal serotype titers re-measured. ANOVA with pre and post antibody titers as the within groups variable will be primary method of data analysis. Nonparametric rank-sum test will be used to compare the differences in antibody titers between the two patient groups. Regression analysis in which the change in antibody titers is the outcome variable will also be used.

**Progress:** Sixty-eight subjects agreed to participate in the study. Urine methylmalbate levels were measured using GC-mass spectrometry. None were found to have B<sub>12</sub> deficiency so none was eligible to continue in the study. Therefore, the study was terminated.



### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol No.:** 96/070      **Status:** Completed

**Title:** Optimal Bowel Preparation for Flexible Sigmoidoscopy: Hypertonic Phosphate Enemas with and Without Use of Oral Magnesium Citrate or Tap Water Enemas

**Start Date:** 02/16/96      **Est. Completion Date:** Mar 97

**Department:** Medicine/Internal Medicine      **Facility:** MAMC

**Principal Investigator:** CPT Eric M. Osgard, MC

<b>Associate Investigators:</b>	MAJ David J. Waddell, MC
CPT Jeffrey S. Strong, MC	LTC Amy M. Tsuchida, MC
MAJ John G. Carrougher, MC	MAJ Kazunori Yamamoto, MC
LTC Robert H. Sudduth, MC	

**Key Words:** Sigmoidoscopy, enemas:hypertonic phosphate, enemas:oral magnesium citrate, enemas:tap water

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	<b>OMA Cost:</b>	
\$0	\$0.00	9/30/97

**Study Objective:** The primary objective of this project is to study the effect of addition of oral magnesium citrate to a standard two enema flexible sigmoidoscopy preparation, and to confirm prior work which has shown no advantage of a two enema preparation over a one enema preparation.

**Technical Approach:** A direct comparison of the commonly used regimens that are proposed in the current study has not been reported. A power analysis was performed using data reported comparing one versus two HPEs, again, which revealed no statistical difference. A 25% difference in rated preparation quality was felt to be clinically significant by the investigators, generating an estimate of 50 patients required per group, based on a total of 2 groups. Since this study will involve three groups, we estimate needing approximately 75-100 patients per group. We plan to perform an initial analysis after 75 patients are done in each group. The particular regimen that patients receive is dependent primarily on the institution to which they present. Thus, the regimen performed is based primarily upon the biases of the endoscopist or nurse educators. The proposed study should provide information upon which a scientifically based recommendation can be made regarding the need to perform an additional enema, or to add oral magnesium citrate.

**Progress:** 163 patients were randomized. Patients receiving the two enemas and a bottle of magnesium citrate had a significantly better preparation, with more studies rated as excellent or good, greater depth of insertion of the sigmoidoscope, and shorter procedure duration. All three groups had equal levels of satisfaction, ease of procedure and ease of preparation with a slightly higher rate of mild diarrhea in the group randomized to receive the magnesium citrate.

The principal investigator was changed to Dr. Osgard from Dr. Jeffrey Strong.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/109	<b>Status:</b> On-going
<b>Title:</b> Coronary Artery Calcification Detected with Computed Radiography as a Marker for Obstructive Coronary Artery Disease		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> Dec 96	
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Principal Investigator:</b> LT Eric B. Stuart, MC		
<b>Associate Investigators:</b> MAJ Christopher A. Meyer, MC CPT Jeffrey S. Strong, MC		MAJ Michael D. Eisenhauer, MC CPT Donald M. Collins, MC
<b>Key Words:</b> coronary artery disease, calcification, computed radiography		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: 1) To determine if chest radiography using a computed radiographic system (MDIS) can detect coronary artery calcification which correlates with significant coronary artery obstruction by cardiac catheterization. 2) To determine if non-radiologists can interpret a computed chest x-ray image for coronary artery calcification with a clinically significant level of accuracy.

Technical Approach: Approximately 200-300 patients presenting to the cardiology service who are referred for coronary catheterization will be asked to participate. All patients undergoing coronary angiography will have their screening computed chest radiograph reviewed for evidence of coronary artery calcification. During the coronary angiography procedure, just prior to the injection of radiocontrast dye into the coronary arteries, a fluoroscopic view of the heart will be recorded on film. The sensitivity and specificity of coronary artery calcification detected by computed chest radiography, by fluoroscopy, and by the combination of the two, will be compared to the detection of obstructive coronary artery disease by coronary angiography. Comparisons and likelihood ratios will be used to evaluate data and most will be presented in table format.

Progress: 100 subjects have been entered in FY 97, pending review of chest x-rays and data analysis.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE  
NEUROLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/007		<b>Status:</b> Terminated	
<b>Title:</b> Ophthalmic Anesthesia in Trigeminal Neuralgia					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Medicine/Neurology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Gary W. Beaver, MC					
<b>Associate Investigators:</b>			MAJ Eugene F. May, MC		
<b>Key Words:</b> Neuralgia, anesthesia, proparacaine					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To investigate the benefit of ophthalmic anesthesia in the treatment of trigeminal neuralgia.

**Technical Approach:** This study will be a double-blind, placebo-controlled trial at multiple military medical centers. Approximately 80 patients will be enrolled study wide, with 25 planned for entry at MAMC. Patients will be randomly assigned to either the test or placebo group. Two drops of either 0.5% proparacaine or saline will be placed onto the cornea ipsilateral to the neuralgia. Patients will receive an additional two drops on day 7 and day 14. Prior to treatment, each patient will be asked her/his frequency of pain attacks and pain severity, and patients will be contacted by phone on days 3, 10, and 30 to collect follow-up data on pain frequency and severity.

**Progress:** The study was terminated due to limited patient enrollment. The criteria for entrance were too constricting. Patients were required to have refractory trigeminal neuralgia to standard of care medicines. One patients was entered and did notice decreased severity and frequency of attacks. The study may have been more successful in patient enrollment if criteria allowed enrollment of patients with some atypical features of trigeminal neuralgia. Also some patients who had failed one medicine did not wish to use the eye drops.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/137		<b>Status:</b> On-going
<b>Title:</b> Clinical Experience and Use of Vigabatrin (Sabril) in Patients with Infantile Spasms				
<b>Start Date:</b> 09/19/97		<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jodie L. Bolt, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Infantile spasms, vigabatrin, open label, dose-ranging, safety, efficacy				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
			<b>Periodic Review:</b> 9/30/97	

**Study Objective:** 1) Assess if patients with infantile spasms treated with vigabatrin become infantile spasms free within the first fourteen days of therapy; 2) assess changes in seizure frequency of infantile spasms and other seizure types prior to and during a treatment period of at least one month and up to three years; 3) assess if pretreatment with vigabatrin alters responsiveness to subsequent antiepileptic drug therapy; 4) gain medical experience using vigabatrin in a patient population and clinical setting not extensively studied in the past; 5) document the time course and resolution of any adverse events; and 6) assess the physician's and caregiver's global assessment at specified visits.

**Technical Approach:** Vigabatrin (Sabril) is an irreversible inhibitor of GABA-transaminase, which catalyzes the catabolism of GABA, an important central nervous system inhibitory neurotransmitter. Vigabatrin is investigational and will be used under IND #47,707 which is held by Hoechst Marion Roussel, Inc. This is a multicenter, open-label, dose-ranging, long-term study of patients with new onset infantile spasms. Up to 150 patients may be enrolled in this study. The duration of this study will be approximately three years. Patients should enroll in this study with the expectation that they will be treated with vigabatrin for a minimum of one month. Appropriate statistical comparison to baseline for seizure control and adverse events will be made.

**Progress:** Awaiting CIRO approval to start.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/083		<b>Status:</b> On-going
<b>Title:</b> Compassionate Use of Vigabatrin in Infantile Spasms				
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Apr 02	
<b>Department:</b> Medicine/Neurology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Jodie L. Bolt, MC				
<b>Associate Investigators:</b>			Letitia Steigerwald	
<b>Key Words:</b> Infantile spasms, Vigabatrin				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: 1) Continuation of compassionate use IND of vigabatrin for 2 patients as an official MAMC Clinical Investigation Protocol; 2) effective control of infantile spasms; and 3) to gain experience in the use of vigabatrin, a promising drug for infantile spasms which is used regularly outside of the U.S. and is undergoing FDA review for commercial marketing in this country.

Technical Approach: Infantile spasms are a severe epileptic encephalopathy associated with significant morbidity and mortality. Vigabatrin is becoming the first line therapy for infantile spasms in countries outside of the U.S. due to its efficacy, tolerability, and decreased morbidity compared to ACTH, the current standard of care in the U.S. Vigabatrin may have even greater benefit (and therefore greater indication for use) in certain selected patients. Patients with symptomatic infantile spasms due to Tuberous Sclerosis are especially responsive to Vigabatrin. Patients with certain inborn errors of metabolism and infantile spasms might be at higher risk from conventional therapies than Vigabatrin. The purpose of this protocol, Compassionate Use of Vigabatrin in Infantile Spasms, is to continue compassionate use of vigabatrin in two patients, one in each category listed above. An FDA IND is held for these two patients and under this protocol, the medication would be continued up to 36 months after initiation, with option to continue if the patients develop seizure types for which vigabatrin could be effective.

Progress: No subjects were entered in FY 97, a total of 2 subjects have been entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/129		<b>Status:</b> Terminated	
<b>Title:</b> The Assessment of Motor Recovery After Stroke Induced Hemiplegia					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b> Aug 94		
<b>Department:</b> Medicine/Neurology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jonathon Newmark, MC					
<b>Associate Investigators:</b>			CPT Eric I. Hassid, MC		
<b>Key Words:</b> hemiplegia, stroke, motor recovery					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

Study Objective: We hope to determine whether or not there exist certain consistent patterns of motor recovery after stroke. We also hope to be able to prognosticate about extent of motor recovery with relation to lesion site and size.

Technical Approach: Select patients from the neurology service who have sustained their first non-hemorrhagic stroke affecting motor function will obtain an MRI of the brain at about the 7 day post event mark for purposes of accurate neuroanatomical localization. These patients will be evaluated weekly to assess motor recovery. No additional studies which would not be part of good stroke care will be done. Clinical and statistical significance will be done by a statistician. The initial data analysis will be longitudinal, modeled upon that of Twitchell. Should trends develop of statistical significance, standard tests including ANOVA will be used as data points.

Progress: No additional patients were entered in FY 97. Previously 15 patients had been entered. Ten had hemipareses that were mild enough to begin with that they made rapid recoveries, in so a short time span that no conclusions could be made. Five patients were followed from almost complete hemiparesis to either plateau (death or most complete recovery they could make). That was nice information, but not enough to make any conclusions since they represented 3 different stroke types. Dr. Newmark terminated the study when he was reassigned.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF MEDICINE,  
PULMONARY SERVICE**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/057		<b>Status:</b> On-going	
<b>Title:</b> The Use of Ipratropiumn Bromide (Atrovent) in COPD Exacerbation					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC William E. Caras, MC					
<b>Associate Investigators:</b> Michael G. Winter, RRT			LTC Thomas A. Dillard, MC		
<b>Key Words:</b> COPD, iratropium, albuterol					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The objective of our protocol is to perform a head to head comparison of nebulized albuterol and ipratropium in hospitalized patients with COPD exacerbation. We plan to use the maximum recommended daily doses of each drug dosed every four hours (ipratropium bromide 350 µg unit every four hours vs albuterol 3.5 mg every four hours)

**Technical Approach:** Major outcomes will include the FEV-1. We will obtain repeated measures in each patient. Ultimately, we wish to determine if there is any significant change in FEV-1 at 24 and 48 hours between treatment groups. We would also like to determine if the initial FEB-1 (<40% or >40%) has any bearing on treatment response. We plan to apply a t-test with data obtained at the 24 hour study interval. If enough patients are still on the protocol at 48 hours, we will apply the ANOVA for repeated measures, but we do not know how many patients will be available for analysis after 24 hours. Clinical outcomes will include length of stay as well as change in respiratory rate, pulse oximetry, VAS, at 24 and 48 hours. The limit of statistical significance will be taken at p=0.05.

**Progress:** Has not started, will start 6 Oct 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 90/099	<b>Status:</b> On-going
<b>Title:</b> Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure		
<b>Start Date:</b> 08/17/90	<b>Est. Completion Date:</b>	
<b>Department:</b> Medicine/Pulmonary	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Donald M. Collins, MC		
<b>Associate Investigators:</b> CPT Stephen M. Salerno, MC		LTC William H. Cragun, MC
<b>Key Words:</b> pleural effusion,albumin,congestive heart failure		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To determine if the albumin gradient is a more effective criterion than Light's criteria to distinguish transudates from exudates in patients with congestive heart failure that have been treated with diuretics.

Technical Approach: Fifteen patients with clinically suspected congestive heart failure and chest radiograph evidence of pleural effusion will be studied. A thoracentesis to remove 50 cc of fluid will be performed and the following laboratory tests will be done on the fluid: albumin, total protein, glucose, LDH, bilirubin, cell count with cyto-spin differential, gram stain, and routine culture. A simultaneous sample of serum will be measured for albumin, total protein, LDH, bilirubin, and glucose. After three to five days of therapy for the congestive heart failure a repeat chest radiograph with bilateral decubitus view will be done. If pleural fluid persists, a repeat thoracentesis and laboratory tests will be done. If no fluid persists after three to five days, then the patient will be dropped from the study. Bilirubin ratio will also be assessed. The classification of the patients as exudate or transudate by serum effusion, bilirubin ratio, and Light's criteria will be compared between the two thoracentesis. McNemar's test for matched-pair data will be used to compare the albumin gradient results to Light's criteria.

Progress: 8 subjects were enrolled in FY 97, for a total of 25 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/076		<b>Status:</b> Completed	
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Pulmicort (Budesonide) Turbuhaler, 400 mcg Administered Once Daily for 12 Weeks, in Adult Patients with Inhaled Steroid....					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Thomas A. Dillard, MC					
<b>Associate Investigators:</b> LTC Thomas A. Dillard, MC LTC William E. Caras, MC Ravi Ramakrishna, M.D.			CPT Kurt W. A. Grathwohl, MC MAJ Timothy R. Murray, MC CPT Cynthia L. Clagett, MC		
<b>Key Words:</b> Asthma, steroid dependent, budesonide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** 1) To compare the efficacy and safety of once daily administered of Pulmicort Turbuhaler, versus placebo, in adult patients aged 18 years or greater with inhaled steroid-dependent asthma. 2) The primary efficacy variable for this study will be mean change from baseline in forced expiratory volume in one second (FEV<sub>1</sub>) over the 12-week treatment period. 3) Secondary efficacy variables will be mean change from baseline in morning and evening peak expiratory flow (PEF), patient discontinuation rates.

**Technical Approach:** This is a multicenter randomized, double-blind, placebo-controlled, parallel group study. The study consists of two phases: a two-week baseline phase followed by a 12-week treatment phase with patients reporting to the clinic six times (at weeks -2, 0, 2, 4, 8 and 12,  $\pm 3$  days) for visits. Male and female outpatients, aged 18 years or greater, with a history of asthma who have been treated with an inhaled corticosteroid for at least the previous 16 weeks will be eligible for enrollment into the baseline phase of the study. On entry into the baseline phase (Visit 1), patients will undergo screening tests, including pulmonary function and reversibility testing. To be eligible for randomization, patients must have an FEV<sub>1</sub> of  $\geq 65\%$  and  $\leq 90\%$  of predicted and a  $\geq 12\%$  increase in FEV<sub>1</sub> following administration of two to four puffs of an albuterol (Proventil®) pMDI with or without a spacer. On entry into the treatment phase (Visit 2) patients will be randomized to receive in a double-blind manner one of two treatments: Pulmicort Turbuhaler 400  $\mu$ g (administered as 200  $\mu$ g of budesonide per inhalation x2 inhalations) or placebo, each administered once daily in the morning for the duration of the 12-week treatment phase. Patients will record peak flow meter values twice a day and maintain a diary of their symptoms. At each study visit, pulmonary function testing will be done, adverse events and diary completion will be assessed, and a pregnancy test will be done if applicable. A quality of life assessment will be completed at visits 2, 4, and 6.

**Progress:** No patients were enrolled at MAMC. The study was terminated at MAMC due to insufficient patient accrual.

The principal investigator was changed from Dr. Timothy Murray to Dr. Dillard in June 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/087		<b>Status:</b> On-going
<b>Title:</b> A Phase 2 Study to Determine the Safety, Pharmacokinetics, and Effective Dose Range and Dosing Duration for Recombinant Activated Protein C (rAPC) in Severe Sepsis				
<b>Start Date:</b> 04/18/97		<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Medicine/Pulmonary		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ George N. Giacoppe Jr., MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Sepsis, recombinant activated protein C				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** 1) To assess the safety of administration of rAPC as a function of dose and dose duration; 2) to determine the degree to which the coagulation abnormalities of severe sepsis are affected by the administration of rAPC as a function of dose and dose duration; and 3) to determine the effective dose and dose duration of rAPC administration, based on the ability of rAPC to alter the coagulation abnormalities of severe sepsis, for use in a future Phase 2 protocol.

**Technical Approach:** This Phase 2 study seeks to demonstrate the safety and pharmacokinetics of rAPC, as well as identify the effective dose range and dose duration of rAPC in the correction of sepsis-induced intravascular coagulation and in the prevention or improvement of sepsis-induced organ failure. rAPC will be administered as a continuous intravenous infusion. This study will be conducted in two sequential steps designated as Stage 1 and Stage 2. Both Stage 1 and 2 are double-blind, placebo-controlled, dose-ranging studies of rAPC administered as a continuous intravenous infusion over a fixed interval of 48 hours (Stage 1) and 96 hours (Stage 2). The initial rAPC dose used in Stage 1 will be based on the doses capable of correcting the coagulation abnormalities seen in hereditary protein C-deficient (HPCD) patients. The initial rAPC doses used in Stage 2 will be chosen from the safest and most efficacious dose of all doses evaluated in Stage 1. After patients are determined to meet eligibility criteria and the patient (or next of kin) has consented to participation, patients will be randomized. Dose and length of infusion will be determined by what stage the study is in. Patients will have frequent assessments and both local and central lab work. A bedside aPTT analyzer will be used to adjust the dosage of study medication. Patients will be followed throughout their hospitalization and at Day 28. All study participants will also receive standard of care treatment with antibiotics and other supportive measures.

**Progress:** Have not started data collection, have completed initiation visit and awaiting an inservice on aPTT monitor.

### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol No.:** 96/138      **Status:** Suspended

**Title:** Active Inspiration/Expiration versus Tidal Volume Breathing During Transbronchial Biopsy

**Start Date:** 08/16/96

**Est. Completion Date:**

**Department:** Medicine/Pulmonary

**Facility:** MAMC

**Principal Investigator:** CPT Kurt W. A. Grathwohl, MC

**Associate Investigators:**

MAJ Timothy R. Murray, MC

MAJ Bernard J. Roth, MC

Suzette Gagnon-Bailey, M.D.

LTC Thomas A. Dillard, MC

**Key Words:** Transbronchial biopsy, inspiration, expiration breathing method, tidal volume breathing method

**Accumulative**

**Est. Accumulative**

**Periodic Review:**

**MEDCASE Cost:**

\$0

**OMA Cost:**

\$0.00

9/30/97

**Study Objective:** To compare yield, results and complications of two currently used techniques for transbronchial biopsy.

**Technical Approach:** All patients referred in the pulmonary clinic for bronchoscopy will be enrolled. Bronchoscopy will be performed in the usual manner. Patients will have a minimum of 6 transbronchial biopsies performed. They will be randomized to have the first three biopsies performed by either the active inspiration/expiration method or the tidal volume breathing method. After 3 biopsies are performed, the patient will be crossed over to the method not previously performed to obtain the next three biopsies. If more biopsies are needed, the attending physician can utilize any method at their discretion although the subsequent biopsy samples will not be included in data analysis. The attending pulmonologist or nurse will record the number of attempts for each and the appearance and quantity of sample grossly. Hemorrhage, pain, dyspnea, change in vital signs, and need for stopping the procedure will be recorded after each attempt. Two containers will be identified to the investigators although the examining pathologist will be blinded to the method performed. The pathologist will identify the number and size of samples in each as well as note the presence of alveolar tissue and the pathologic diagnosis if any. We will enroll 100 patients over one year. The differences between number of adequate samples and size will be compared using the paired student t-test. Other variables such as presence of alveoli and presence of complications (i.e. chest pain, bleeding, dyspnea, etc.) will be compared using the chi square test.

**Progress:** No patients were entered in this study prior to the transfer of Dr. Grathwohl. It has been put in a suspended status until a new principal investigator is assigned.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/029		<b>Status:</b> On-going	
<b>Title:</b> A Prospective Study Using the Airway Occlusion Pressure (PO.1) To Predict the Outcome of Weaning From Mechanical Ventilation					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> May 94		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kurt W. A. Grathwohl, MC					
<b>Associate Investigators:</b>			MAJ James D. Pike, MC		
MAJ George N. Giacompe Jr., MC			MAJ Francis J. Landry, MC		
CPT Jeremy R. Blanchard, MC			MAJ Lewis L. Low, MC		
<b>Key Words:</b> ventilation, airway occlusion pressure					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		9/30/97
			\$0.00		

**Study Objective:** The main objective of this study is to ascertain the usefulness of the PO.1 as a weaning parameter in predicting success or failure of patients upon extubation. The secondary objective is to validate the Rapid Shallow Breathing Index as described by Yang and Tobin.

**Technical Approach:** Weaning parameters will be obtained and documented by a Respiratory Care Practitioner (RCP) on patients in the surgical and medical ICU at MAMC. Individual progress toward weaning and extubation will be determined by the primary physician/team. When it is determined the patient is ready for extubation, a second set of weaning parameters will be obtained immediately prior to extubation. Weaning parameters will only be collected on patients at rest and who have not been stimulated within the prior 10 minutes. The parameters will be obtained by utilizing the Respiratory Mechanics Package on the Infrasonics Adult Star as required by MAMC policy. Only the data obtained from patients on the Infrasonic Adult STAR mechanical ventilator will be used so that our results are reproducible since other available ventilators do not easily measure the PO.1. The first 50 patient's will be used to form ROC curves to develop threshold values for the prediction of success or failure of extubation which can then be prospectively applied. A successful weaning/extubation will be defined as one in which the patient does not have to be reintubated within 24 hours.

**Progress:** Previously, approximately 70 had been entered. This data was considered to be potentially biased due to incorrect blinding procedures, plus it was lost upon the transfer of Dr. Grathwohl. Dr. Dillard was named as the principal investigator in May 97. He has decided to restart the protocol using new patients and rebuild the data base. Ten patients were entered in the new data base in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/004		<b>Status:</b> Terminated	
<b>Title:</b> Controlled Prospective Evaluation of Intrapulmonary Percussive Ventilation with Standard Chest Physiotherapy					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Nora A. Regan					
<b>Associate Investigators:</b> Michael G. Winter, RRT			MAJ Timothy R. Murray, MC LTC Thomas A. Dillard, MC		
<b>Key Words:</b> Pulmonary percussive ventilation, standard chest physiotherapy, secretions, atelectasis, complications					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		10/18/96	

**Study Objective:** To compare the effectiveness of Intrapulmonary Percussive Ventilation (IPV) with standard Chest Physiotherapy (CPT) for treatment of lobar atelectasis or secretion mobilization in patients with compromised clearance mechanisms.

**Technical Approach:** Two hundred patients having immobile airway secretions who are ordered for CPT will be randomly assigned to receive either standard CPT or IPV therapy. IPV therapy is the delivery through the mouth of high-frequency oscillations in air flow, combined with in-line nebulization of beta agonist or normal saline. Major endpoints will be spirometry parameters, oxygenation, sputum production (amount and characteristics) and radiographic changes as well as duration of treatments and RT workloads.

**Progress:** Eight patients were entered. After approximately a 12-month attempt, the number of patients with a neurologically stable condition that required PT and who could give consent was insufficient to perform the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 91/015		<b>Status:</b> On-going	
<b>Title:</b> Controlled Trial of Positive Pressure Ventilation via Nasal Mask in Patients with Severe Chronic Air Flow Obstruction and Chronic Respiratory Failure					
<b>Start Date:</b> 12/07/90			<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Bernard J. Roth, MC					
<b>Associate Investigators:</b> MAJ Bruce S. Grover, MC			LTC William H. Cragun, MC		
<b>Key Words:</b> positive pressure ventilation,air flow obstruction,nasal mask					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$260.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine if one eight hour period per week of ventilatory rest via nasal mask positive pressure ventilation will improve pulmonary function and exercise tolerance in patients with chronic air flow obstruction and chronic respiratory failure marked by an elevated arterial carbon dioxide.

**Technical Approach:** The study population will be both sexes, age >18 years, with severe COPD. The following baseline values will be obtained: age, weight, height, smoking status, medication list, chest x-ray, spirometry, formal lung volumes, MIP, MEP, DLCO, arterial blood gas measurement, pulse oximetry, end-tidal capnography, thyroid function tests, CBC, electrolytes, Karnofsky scale, dyspnea index, and 12 minutes walking distance. Spirometry, pulse oximetry, and end-tidal capnography will be repeated once weekly for four weeks. After four weeks, baseline studies will be repeated and an overnight polysomnography will be performed which includes electroencephalogram, electromyogram, electro-oculogram, airflow, chest wall and abdominal motion, pulse oximetry, and transcutaneous capnography. At this time the patient will be tested to determine if he tolerates intermittent positive pressure ventilation through a nose mask (nIPPV). Patients who tolerate nIPPV will be randomized to once weekly overnight nIPPV or nasal continuous positive airway pressure (nCPAP). Every 4 weeks during the 12 weeks of treatment, a repeat baseline evaluation will be done except that a transition dyspnea index rather than a baseline dyspnea index will be obtained. After 12 weeks of active therapy, the patients will be followed for an additional 12 weeks with 4 week evaluations as in the previous 12 weeks. Any change in pulmonary function, exercise tolerance, or dyspnea index will be compared between nCPAP and nIPPV patients using Student's T-test. Significantly improved exercise tolerance, subjective dyspnea, Karnofsky scale, MVV, MIP, MEP, FVC, or PaCO<sub>2</sub> will be considered a positive result of nIPPV.

**Progress:** No subjects have been entered in FY 97.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/132		<b>Status:</b> On-going	
<b>Title:</b> Respiratory Care Team to Decrease the Misuse of Metered Dose Inhalers in Hospitalized Patients					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Bernard J. Roth, MC					
<b>Associate Investigators:</b> MAJ Timothy R. Murray, MC Nora A. Regan			CPT Kurt W. A. Grathwohl, MC Michael G. Winter, RRT		
<b>Key Words:</b> Inhaler, metered dose, proper use					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine if a respiratory team teaching proper metered dose inhaler (MDI) use to inpatients will improve the observed rate of proper MDI use at Madigan Army Medical Center (MAMC).

**Technical Approach:** In this study, a pulmonologist will interview 60 inpatients prescribed an MDI and observe their MDI technique to establish a baseline rate of misuse. Then a respiratory care team will receive a daily list from Pharmacy on all patients newly prescribed an MDI. They will provide direct teaching to the patients on correct use of their MDI. After the teaching program has been in place for 2- 6 weeks the same pulmonologist will interview 60 more patients and observe their MDI technique to establish the rate of misuse after the intervention. The patient will be asked if they have received education and this will be correlated to the chart documentation of education by the Respiratory Therapist. The major endpoint will be the change in the rate of MDI misuse observed.

**Progress:** The protocol has been approved but not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/172		<b>Status:</b> Completed	
<b>Title:</b> The Value of Questionnaire Responses and Body Measurements in the Prediction of Obstructive Sleep Apnea in a Young Physically Fit Population					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Bernard J. Roth, MC					
<b>Associate Investigators:</b> MAJ Joseph D. Kern, MC			Vishesh Kapur, M.D.		
<b>Key Words:</b> Sleep apnea, questionnaire. body measurements					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** This study has two primary aims: to determine the prevalence of various symptoms and their specificity in obstructive sleep apnea syndrome (OSAS), and to examine the association of neck circumference, body mass index (BMI) and specific symptoms with sleep disordered breathing. Secondary aims are to determine if hypothyroidism needs to be excluded in individuals from this population being evaluated for OSAS, and to estimate period prevalence of OSAS in this population.

**Technical Approach:** Consecutive patients between the ages of 18 to 35 referred to MAMC for polysomnography will be eligible for inclusion in this cross sectional study. 200 eligible consenting participants will complete a symptom questionnaire and undergo a brief examination that includes neck circumference, blood pressure, weight and height measurements, and have serum thyroid stimulating hormone (TSH) evaluation prior to overnight polysomnography. An equal number of controls randomly sampled at routine health visits will complete the symptom questionnaire and have neck circumference, weight and height measurements performed. Questionnaire responses and anthropometric measurements will be compared between patients with OSAS and patients without OSAS and controls using the student's t-test at  $\alpha=0.05$ . Sensitivity and specificity will be calculated for questionnaire responses. Questionnaire responses along with BMI, neck circumference (corrected for height), and hypertension will be evaluated using multiple linear regression techniques using apnea hypopnea index as the dependent variable. In addition, each of these factors will be evaluated individually by simple linear regression. The r and slope obtained for corrected neck circumference and BMI from linear regression will be compared with previously published estimates from other populations using the t-test. The prevalence of hypothyroidism in all patients evaluated by polysomnography and just those with OSAS will be compared to the estimated prevalence in this age group (0) and the prevalence at a which screening for hypothyroidism is commonly recommended (2-5%) using the student's t-test. A period prevalence will be calculated by dividing the number of cases detected in one year by the total referral population.

**Progress:** Fifty patients and 50 controls were entered in this study at MAMC. The data are being analyzed at the University of Washington.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 92/024		<b>Status:</b> On-going	
<b>Title:</b> Resectable Bronchogenic Carcinoma: Value of Routine Contrast - Enhanced Cranial MRI in Preoperative Staging					
<b>Start Date:</b> 01/03/92			<b>Est. Completion Date:</b>		
<b>Department:</b> Medicine/Pulmonary			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Bernard J. Roth, MC					
<b>Associate Investigators:</b>			MAJ Kevin L. Quinn, MC		
LTC Miquel J. Rovira, MC			LTC Steven S. Wilson, MC		
MAJ Frank A. Zimba, MC					
<b>Key Words:</b> cancer, bronchogenic, MRI					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

Study Objective: To determine the incidence of clinically occult brain metastasis in patients with resectable primary bronchogenic carcinoma.

Technical Approach: The subjects (100) for this protocol will be patients >18 years of age with primary bronchogenic carcinoma, Stage IIIa or less as determined by chest CT, who are neurologically intact. The patient will undergo a complete clinical neurological history and physical exam and enhanced cranial MRI to screen for brain metastasis. Patients with evidence of significant CNS pathology will be divided into four groups: (1) solitary lesion amenable to neurosurgical resection (2) significant brain pathology other than metastatic disease that would delay or preclude therapy (3) brain metastasis and (4) metastasis outside the brain. Patients in group 1 or 2 will undergo neurosurgical and/or radiation therapy evaluation for possible curative or palliative therapy. Patients in group 3 or 4 will undergo radiation therapy and/or hematology-oncology evaluation for possible palliative therapy. Patients in whom MRI revealed suspicious areas which are not definitely characteristic for metastasis will undergo brain biopsy using stereotactic localization. Patients refusing brain biopsy will be followed closely with periodic follow-up enhanced cranial MRI every three months. MRI and clinical data will be evaluated to determine the overall incidence of clinically occult brain metastases and the presence (if any) of any significant differences among primary cell types.

Progress: 4 subjects have been entered in FY 97.

DETAIL SHEETS FOR PROTOCOLS

DEPARTMENT OF NURSING

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/067		<b>Status:</b> Terminated
<b>Title:</b> Increased TMC Access to Urinary Incontinence Therapy				
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Dec 98	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Ann M. V. Bianchi, AN				
<b>Associate Investigators:</b> COL Gary D. Davis, MC			LTC Richard A. Sherman, MS	
<b>Key Words:</b> Urinary Incontinence, access, troop medical clinic				
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** Determine whether bringing a treatment for urinary incontinence from the medical center environment to the troop medical clinic environment increases its utilization while maintaining effectiveness.

**Technical Approach:** Our current survey of all female soldiers in field units at Fort Lewis has shown that nearly one-third of female soldiers have significant problems with exercise-induced urinary incontinence. The study showed that (a) combination of biofeedback and pelvic floor muscle exercise ("Kegels") are very effective for treatment of exercise-induced urinary incontinence among female soldiers, (b) that these soldiers will not perform Kegel exercises without significant prompting, and (c) that most of them simply cannot get the required treatments because their jobs interfere with their getting to a major medical center. The proposed project is a follow-on to this very successful study on use of vaginal biofeedback for treatment of urinary incontinence among female soldiers. We propose to perform a study designed to bring this treatment from the medical center environment into the troop environment. This will be accomplished by having a portable biofeedback system (and skilled therapist required to use it) visit each of the five troop clinics at Fort Lewis with large populations of female soldiers once per week. All female soldiers at Fort Lewis will be surveyed about availability of urinary incontinence treatment, and the feasibility of using it, both before and after the portable unit is made available at troop clinics. Thus, it is clear that (a) there is a real need to treat our soldiers for urinary incontinence, (b) that an effective, simple, non-invasive treatment exists, and (c) our soldiers cannot get the care they need because it is not offered in a place they can get to. We propose to determine whether bringing the treatment to the troops increases its utilization while maintaining effectiveness.

**Progress:** This protocol was terminated because it did not receive grant funding. No patients were entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/003		<b>Status:</b> Completed	
<b>Title:</b> Effect of Prophylactic Preoperative Intravenous Caffeine Administration on the Incidence of Postoperative Headache in the Daily Caffeine User					
<b>Start Date:</b> 10/18/96			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Joseph B. Chapman, AN					
<b>Associate Investigators:</b>					
CPT Andrew A. Armondo, AN			CPT Bryan P. Hunter, AN		
CPT Nancy L. Sweet, AN			MAJ Connie J. Moore, AN		
			CPT Evelyn J. Williams, AN		
<b>Key Words:</b> Headache:postoperative, caffeine					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** The purpose of this study is to determine whether headaches could be prevented in patients with a consistent daily caffeine intake of  $\geq 200$  mg caffeine, in 100 ml of 0.9% normal saline, on the morning of surgery versus an intravenous saline placebo.

**Technical Approach:** This study will be conducted on ASA I and II patients undergoing elective procedures requiring general anesthesia, who have a daily caffeine intake  $\geq 200$  mg/day. The sample size will be 70 patients. All consenting patients who meet the study criteria will be included in the convenience sample. Patient participation will begin with the completion of a Preoperative Pain Assessment Tool. This tool will assess whether or not the patient reports headache pain prior to surgery. Upon completion of the tool, the researcher will randomly assign the patient to receive either 100 mg of caffeine in 100 ml of 0.9% normal saline or a placebo of 100 ml of 0.9% normal saline intravenously. The caffeine solution will be supplied by the MAMC pharmacy. The administration of either caffeine or the placebo will occur over 30 minutes via an infusion pump prior to surgery. The patient will then go to surgery without change in surgical and anesthetic standards of care. Postoperatively the patient will go to the post anesthesia care unit for routine recovery. When the patient is awake and alert, the post anesthesia care unit nurse will administer the Postoperative Pain Assessment Tool. Upon completion of the tool, the patient's participation in the study will be completed.

When all data has been collected, statistical significance will be examined. Chi Square analysis will be used to examine the relationship between the study's major independent variables (receiving 100 mg of caffeine in 100 ml of 0.9% normal saline or 100 ml of 0.9% normal saline) and dependent variables (whether or not the subject reports having a headache). Multiple regression will be used to measure the possible relationship between various variables (age, sex, length and type of surgery, anesthetics/ medications administered perioperatively, and the amount of daily caffeine consumed) and headache. This will help the researchers to determine whether or not these variables contribute to the incidence of postoperative headache.

**Progress:** Thirty subjects and 30 controls were enrolled in this study. The results indicate that daily caffeine-using patients do not usually present with a postoperative caffeine withdrawal headache early in the recovery period. Therefore, a prophylactic preoperative intravenous dose of caffeine is not necessary. A presentation was made at the 1997 American Association of Nurse Anesthetists National Meeting.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/131		<b>Status:</b> On-going
<b>Title:</b> Risk Factors for Nosocomial Pneumonia				
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Aug 98	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Laura L. Feider, AN				
<b>Associate Investigators:</b> MAJ Roger H. Anderson, AN			MAJ Mary S. McCarthy, AN	
<b>Key Words:</b> Nosocomial pneumonia, risk factors				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
				<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine risk factors for nonsocomial pneumonia development in ICU patients; and to determine whether the variables chosen occurred more frequently in patients who developed nosocomial pneumonia than in those who did not.

**Technical Approach:** This study is a retrospective chart review, using case control design comparing records of ICU patients who develop nosocomial pneumonia to those who do not develop this infection. A chart review will be conducted to gather the data (Appendix B). Associations between the presence of the identified risk factors (physiologic and treatment variables) and the development of nosocomial pneumonia will be analyzed. The control groups will be used to determine whether the variables chosen occurred more frequently in patients who developed nosocomial pneumonia than in those who did not. The study investigator will perform all the chart reviews. The infection control nurse will identify the relevant charts. The data will be recorded on the chart review tool (Appendix B) and then transferred to a computer program by the study investigator. The chart review tool includes questions related to the physiologic and treatment variables (Appendix A). The study endpoints include identification of variables associated with nosocomial pneumonia development for length of stay and mortality rates.

**Progress:** 120 charts have been reviewed during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/078		<b>Status:</b> Completed	
<b>Title:</b> Expert Power and Decision Making in Nurse Managers: A Test of the Theory of Planned Behavior					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Melissa A. Forsythe, AN					
<b>Associate Investigators:</b>			Lori A. Loan, MSN, RNC		
<b>Key Words:</b> Behavior, decision making, nurses					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The objective of this study was to pilot test an instrument designed to measure the antecedents of specific decision making behaviors in Army nurse managers, in order to establish initial reliability and validity for the instrument. A secondary objective was to test the conceptual model forming a basis for the study, to begin to identify the antecedents to effective decision making in this population.

**Technical Approach:** Subjects in this study will include all available Army Nurse Corps officers, within the continental U.S., Alaska, and Hawaii, who are currently assigned to first-level manager positions (Head Nurse or the equivalent), and who have at least six months' experience in such a position. These officers will be identified in consultation with the Chiefs, Department of Nursing of each facility; officers included in the sample will be mailed a copy of the questionnaire, along with a cover letter explaining the purpose of the study. Three weeks after the initial mailing, all subjects will be mailed a reminder/thank you postcard; three weeks later, the non-respondents will be mailed a second packet with a new copy of the instrument. Descriptive statistics will be generated using SPSS for Windows. Confirmatory factory analysis will be used to determine construct validity and structural equation modeling to initially test the conceptual model using AMOS 3.1.

**Progress:** Questionnaires were sent to 364 first-line nurse managers located in 33 medical treatment facilities in CONUS, Alaska, and Hawaii. 293 questionnaires were returned with 289 considered usable. Initial analysis indicated acceptable initial reliabilities for the instrument's subscales (ten subscales had alpha reliabilities ranging from 0.75 to 0.85) and factor analysis demonstrated moderate to strong factor loadings on the hypothesized factors for all but one subscale. Results of the model testing partially supported the relationships hypothesized in the conceptual model, indicating that perceptions of control were more significantly associated with decision making intentions and behavior than personal and social beliefs surrounding such behavior. The variable of expert power did not demonstrate significant relationships with either decision making intents or behavior.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/068		<b>Status:</b> On-going	
<b>Title:</b> Effects of Stress Responses on Wound Healing					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Sep 00		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Stacey L. Heiner, BSN, RN					
<b>Associate Investigators:</b> Heitkemper MM MAJ Susanne J. Clark, AN			JoAnne D. Whitney, Ph.D., RN Lori A. Loan, MSN, RNC		
<b>Key Words:</b> Wound healing, stress, ePTFE, transferrin					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** Compare measures of preoperative and postoperative psychological stress, SNS and HPA activation (STAI, RIES, PSQ-III GSS, urinary norepinephrine, epinephrine and cortisol) in subjects experiencing minor (e.g., outpatient arthroscopic) and major (e.g., total knee arthroplasty) surgical procedures.

**Technical Approach:** The proposed study will use a prospective, correlational design to explore relationships between pre and postoperative psychologic and physiologic stress and the defined wound healing indices. The study will enroll a total of 96 subjects over a three year period from populations experiencing minor and major orthopedic knee surgery. The relationship between each preoperative and postoperative measure of stress and each wound healing measure will be evaluated with the Pearson product moment correlation coefficient. Repeated measures analysis of variance will be used to compare the stress experienced by patients undergoing major surgery to those undergoing minor surgery at the eight times of measure.

**Progress:** Study has not yet begun, recruitment should start in Nov '97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/100		<b>Status:</b> Completed	
<b>Title:</b> Postoperative Wound Healing: Hydration and Oxygenation					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Stacey L. Heiner, BSN, RN					
<b>Associate Investigators:</b>			JoAnne D. Whitney, Ph.D., RN		
Lori A. Loan, MSN, RNC			COL Daniel G. Cavanaugh, MC		
LTC Brenda I. Mygrant, AN			LTC Pamela J. Hildreth, AN		
LTC Blaine R. Heric, MC			Diane M. Pierson, BS, BA, CCRN		
<b>Key Words:</b> wound healing:hydration, wound healing:oxygenation					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					05/16/97

**Study Objective:** To (1) Compare an augmented fluid replacement protocol to a conventional fluid replacement protocol after open-heart surgery for its effects on: a. subcutaneous tissue oxygen levels; b. subcutaneous tissue perfusion; and c. wound healing indicators in wound tissue samples including: 1) hydroxyproline accumulation measured by high pressure liquid chromatography; and 2) cellular composition, fibroblast proliferation and connective tissue as measured by histologic evaluation on postoperative day 7.

**Technical Approach:** This is a randomized 2 group (80 subjects per group) experimental design. The control group will receive the standard protocol for postoperative intravenous fluid. The experimental group will receive fluid augmentation with an additional intravenous infusion of 20 cc/hr of 5% Dextrose in water. The biochemical and cellular markers of healing will be measured 7 days postoperatively. The tissue indicators of oxygen and perfusion will be measured on the day of surgery and for the next 2 postoperative days. Sternal and leg wound assessments will be made for the first five days during hospitalization. For subjects discharged before the 7th postoperative day the ePTFE implant will be removed on the 7th postoperative day during a clinic visit. Descriptive statistics (mean, standard deviation) will be used to summarize sample description variables. Student's t-tests or chi-square analysis will be performed on the variables measured pre-intervention to ensure randomization of the two groups.

**Progress:** Fifty additional subjects were entered in FY 97 for a total of 158. All but 17 of the subjects completed the protocol in its entirety.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/112	<b>Status:</b> On-going
<b>Title:</b> Wound Healing: The Effect of Supplemental Oxygen Therapy		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> Sep 97	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Stacey L. Heiner, BSN, RN		
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC		JoAnne D. Whitney, Ph.D., RN LTC Brenda I. Mygrant, AN
<b>Key Words:</b> Wound healing, oxygen therapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/16/97

**Study Objective:** The aim of nursing research is to maximize positive patient outcomes through research-based nursing interventions. This study will provide a foundation of developing nursing standards based on evaluation of the independent variable, inhaled supplemental oxygen, and it's role in wound healing. Wound healing, a complex phenomenon involving modifiable and non-modifiable person variables, can be affected by research-based nursing interventions.

**Technical Approach:** The proposed pilot study utilizes a randomized, two group experimental repeated measures design. subjects are randomly assigned to either the control or the intervention group using computer generated random number blocks of 6. This assures that there are not large imbalances between groups at any point in the study. The control group will receive only room air, which is current standard therapy. The intervention group will receive supplemental oxygen at 28% in the form of 2 liter per minute via nasal cannula for 36 hours postoperatively. Subjects will be randomized upon admission to the surgical ward. Subjects will be recruited from those who undergo cervical fusion and/or excision of cervical intervertebral disc, either through the Neurosurgery or the Orthopedic Surgery Services. Based on existing data, it is hoped that 24 subjects can be recruited over the one year study period.

**Progress:** 16 subjects were entered during FY 97, for a total of 16 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/077		<b>Status:</b> On-going
<b>Title:</b> Linking Nursing Care to ANA Quality Indicators				
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Sep 98	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Pamela J. Hildreth, AN				
<b>Associate Investigators:</b>			Lori A. Loan, MSN, RNC	
COL Bonnie L. M. Jennings, AN			Elizabeth Pulos, Ph.D.	
Staggers N			Mitchell PH	
<b>Key Words:</b> Quality indicators, patient satisfaction, health care report card				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: 1) To gain a better understanding of our ability to collect the ANA Nursing Quality Indicator data; 2) to assess the feasibility of collecting nursing care quality data and; 3) to examine the existence and strength of relationships between nursing care and the ANA Nursing Quality Indicators.

Technical Approach: Because nurses are an integral part of the health care delivery system, both in terms of patient contact and hospital spending, the ANA has initiated an endeavor to formulate a nursing report card which will include patient-focused outcome indicators chosen for their ability to link nursing care quality to patient-focused outcomes. The links between patient outcomes and the nursing care quality identified by the ANA Nursing Quality Indicators are not well understood. However, before these relationships can be tested, more information about the feasibility of collecting nursing care data and patient outcomes data is necessary. Using a variety of methods including expert panels, chart review and questionnaires, information related to the ANA Nursing Quality Indicators and nursing care quality will be gathered and evaluated. The final goal is to statistically determine whether the ANA Nursing Quality Indicators are sensitive to documented differences in the quality of nursing care patients receive using ANOVA. Further research on indicators sensitive to changes in nursing care quality will potentially improve the quality of patient care by promoting both the science of outcomes research and the practice of nursing. In addition, identifying quality indicators will provide valuable input for balancing administrative and clinical decision making.

Progress: Protocol was recently funded and has not yet started.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/132		<b>Status:</b> On-going	
<b>Title:</b> Pressure Ulcer Prevention: Comparing Support Surfaces					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Sep 99		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Pamela J. Hildreth, AN					
<b>Associate Investigators:</b> LTC Brenda I. Mygrant, AN			LTC Linda H. Yoder, AN Gladys Cobb, BSN, MSN		
<b>Key Words:</b> Ulcer prevention, Kinair bed, EHOB waffle mattress					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** 1) Determine the demographic characteristics that differ between patients who do and those who do not develop pressure ulcers. 2) Compare the incidence of pressure ulcers between the patients on the KinAir® bed and patients on the EHOB WAFFLE® mattress. 3) Determine the difference in length of stay and monetary expenditure for individuals within the two support surface groups who do not develop pressure ulcers. 4) Determine the difference in length of stay and monetary expenditure for individuals within the two support surface groups who do develop pressure ulcers.

**Technical Approach:** The proposed study is a prospective, quasi-experimental design, in which subjects who are at risk for pressure ulcer development will be randomly assigned to one of two support surfaces. Data will be collected for a period of at least one week or until the subject is discharged, expires, or is no longer considered at risk. Data to be collected will include pressure sore risk using the Braden Scale for Predicting Pressure Sore Risk, daily skin integrity assessments, and information on pressure ulcer development and subsequent ulcer progression using the Pressure Sore Status Tool, as well as data on selected demographic variables. The study will be conducted in multi-site settings. The primary site for the study will be Madigan Army Medical Center and Brooke Army Medical Center (BAMC) is the study's secondary site. Using data obtained from the Wound Care Specialists at both MAMC and BAMC, it is anticipated that approximately 4 eligible subjects will be admitted to BAMC per week. Because the proposed study offers daily care from a research team devoted to maintaining skin integrity, a 75% consent rate is predicted. This equates to enrollment of 3 subjects per week at MAMC and 2 per week at BAMC. An attrition rate of approximately 10% is anticipated based on preliminary data from the Tri-Services Nursing Research Group funded study "Pressure Ulcers: Patient Outcomes on Kinair Bed or EHOB Mattress." Recruitment will occur for twenty-eight months and enrollment of 560 subjects is anticipated.

**Progress:** Discussions with Logistics regarding biomedical maintenance and cleaning of the "intervention" bed, the KinAir bed, delayed recruitment until March '97. The aging beds were not expected to remain functional for the duration of the study. At the present time, 2 beds are functional and the study continues to enroll subjects. From January to March all nursing units were inserviced about the study and the intervention surfaces, the KinAir bed and the EHOB Waffle Mattress. Recruitment of 24 subjects thus far at the MAMC site has resulted in no adverse events and widespread acceptance of both support surfaces as key to the prevention of pressure ulcers. To date, 2 patients have developed a pressure ulcer; one on a KinAir bed and one while on a Waffle Mattress. No statistical analysis has been conducted.

Recruitment appears to be affected by low census figures and a shortened length of stay at both study sites, MAMC and Brooke AMC. Communication is ongoing with investigators at Brooke AMC and strategies to optimize recruitment are under discussion.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/122		<b>Status:</b> Terminated	
<b>Title:</b> A Grounded Theory Analysis of Patient Satisfaction in the Military					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Sep 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Bonnie L. M. Jennings, AN					
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC			COL Frances D. Anderson, AN Debra DePaul, RN		
<b>Key Words:</b> Patient satisfaction, military, TRICARE					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					07/18/97

**Study Objective:** The primary purpose of this study is to describe the experiences, expectations, and preferences of military health care beneficiaries, as related to health care in the TRICARE environment. The overall goal of this study is to describe, through grounded theory method, the process by which military health care beneficiaries arrive at their perceptions of satisfaction or dissatisfaction with their health care experience.

**Technical Approach:** The purpose of this study is to generate hypotheses regarding how military health care beneficiaries arrive at their perceptions of their health care experience. Approximately 30 military beneficiaries who reside within the 40 mile MAMC catchment will be purposely selected from the DEERS roster. Theoretical sampling dictates that the variety of experiences existing in the empiric care would will be represented. The sample size, however, will be dictated by ongoing data collection. Subjects will be interviewed to describe their experiences and expectations as they relate to obtaining health care, and to elucidate what level of preferences they will allow as minimally tolerated. All interviews will be audiotaped and transcribed. Data analysis will be done concurrently with the interviews. It will consist of open coding (conceptualizing and categorizing data), axial coding (establishing relationships between categories), selective coding (emergence of the dominant category), and theoretical integration (reflection of the emerging theory and description of the phenomenon under study).

**Progress:** This study did not receive grant funding; therefore, it was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/125		<b>Status:</b> On-going
<b>Title:</b> A Survey of Access to Care in the TRICARE Environment				
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Sep 98	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Bonnie L. M. Jennings, AN				
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC			COL Frances D. Anderson, AN Suzanne K. Wilson, MSN, RN	
<b>Key Words:</b> TRICARE, access to care, Madigan Army Medical Center				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: To describe access to health care in the TRICARE environment.

Technical Approach: Using a stratified sample of 7,680 military beneficiaries from the MAMC 40 mile catchment areas, this descriptive survey aims to describe access to health care in the TRICARE environment. The research questions are: 1) How do military beneficiaries (consumers) in the MAMC 40 mile catchment area evaluate access to health care? 2) How do military beneficiaries in each of the consumer groups evaluate access to health care? 3) How do members of each of the components of TRICARE evaluate access to health care? 4) Do consumer evaluations of access to care differ according to TRICARE component? Randomly selected beneficiaries from the four TRICARE components will complete and return a mailed questionnaire. Instruments selected for use in the study include the PSQ-III, the General Health Perceptions scale from the SF-36, and select sociodemographic questions from the 1994-1995 Annual Health Care Survey for DoD Beneficiaries. The instruments were chosen for their appropriateness and their high levels of reliability and validity. Data from the survey will be analyzed using descriptive statistics and one-way ANOVA.

Progress: Health Affairs approval of survey was denied in Nov 96. An agreement with HA will allow the data from their Annual Health Survey to be used to answer the research questions.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/063		<b>Status:</b> Terminated	
<b>Title:</b> Caregiver Interactions and Patient Satisfaction					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Bonnie L. M. Jennings, AN					
<b>Associate Investigators:</b>			Lori A. Loan, MSN, RNC		
LTC Pamela J. Hildreth, AN			Elizabeth Pulos, Ph.D.		
Staggers N			Mitchell PH		
<b>Key Words:</b> Patient satisfaction, communication, collaboration					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

Study Objective: 1) Establish a successful procedure for collecting caregiver interaction data; 2) establish response rates, means, standard deviations and information about stability-over-time for caregiver interaction data collected in a military medical center; 3) test the correlations between caregiver interactions and patient satisfaction in a military medical center; 4) test the use of the ICU Nurse-Physician Questionnaire in a variety of inpatient care settings in a military medical center; and 5) explore additional transprofessional indicators (covariates or other antecedents) that influence patient satisfaction in a military medical center.

Technical Approach: The study will use a correlation, descriptive, longitudinal design to observe caregiver interactions and patient satisfaction stability or change over time via repeated measurements and to assess the extent to which levels of these variables correlate with one another. A convenience sample of and 500 inpatients will complete the PSQ-IV (a measure of patient satisfaction). Data will be analyzed using descriptive statistics and Pearson correlations.

Progress: This study did not receive grant funding; therefore, it was terminated.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 93/117		<b>Status:</b> Completed	
<b>Title:</b> Exogenous Surfactant Therapy in Premature Infants					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Lori A. Loan, MSN, RNC					
<b>Associate Investigators:</b> LTC Barbara S. Turner, AN LTC Deborah J. Leander, AN			LTC Joanna C. Beachy, MC CPT William D. Glover, AN		
<b>Key Words:</b> surfactant, premature infants					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					05/16/97

**Study Objective:** To examine two types of surfactant (Exosurf & Survanta), 3 methods of administration, and the resulting neonatal physiologic responses and outcomes. A secondary aim will be to determine the relationships between type of surfactant and administration technique, nursing assessed neonatal clinical cues of a hemodynamically significant patent ductus arteriosus, and neonatal outcomes.

**Technical Approach:** This is a prospective, quasi-experimental study, in which selected physiologic parameters will be monitored during exogenous surfactant administration in a convenience sample of 24 premature infants. Subjects will be randomly divided into one of three administration groups. A control group receiving no surfactant would not be appropriate as it would mean the infants would receive less than the standard of care.

The convenience sample will consist of 24 neonates, with the diagnosis of RDS, who will receive exogenous surfactant using rescue therapy. The three groups will be: 1) n=12, Exosurf administered by sideport adapter. 2) n=6, Survanta administered by feeding tube through endotracheal tube. 3) n=6, Survanta administered through double lumen ET tube. After consent is obtained and electronic monitors applied, baseline data will be collected for 10 minutes after which either Survanta or Exosurf will be administered by the predetermined route. The infant will be ventilated during the procedure using NICU SOPs. At completion of the surfactant administration, data collection will continue for 2 hours. Nurses will be free to make whatever adjustments they deem necessary in response to the lung compliance changes using their own judgment or in consultation with the physician.

Descriptive statistics obtained from the data will be categorized into critical ranges for each of the data collection periods. Demographic data will be coded and analyzed.

**Progress:** Sixty subjects were entered in the study. Data analysis is complete and a final report has been submitted to the TriService Nursing Research Group.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/175	<b>Status:</b> Completed
<b>Title:</b> A Comparison of Skin Microbes Under Two Types of Temperature Probe Covers Used on Premature Newborns		
<b>Start Date:</b> 08/18/95	<b>Est. Completion Date:</b> Sep 96	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Lori A. Loan, MSN, RNC		
<b>Associate Investigators:</b>		
MAJ Pamela S. Birgenheier, AN		Debra DePaul, RN
Suzanne K. Wilson, MSN, RN		CPT Wade K. Aldous, MS
<b>Key Words:</b> Microbes, probe covers, NICU		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/16/97

**Study Objective:** This is a descriptive pilot study to determine if the temperature probe covers in current use in the NICU contribute to nosocomial infections by providing an environment for normal skin microbes to colonies.

**Technical Approach:** Two types of probe covers are currently used in the MAMC NICU. One type has a reflective exterior surface and a type of foam tape adhesive on the interior surface (Probe Cover A). The second type also has a reflective exterior but has a hydrogel adherent surface (Probe Cover B). Probe covers will be placed on 20 premature newborns (28 to 34 weeks gestational age) following their first bath, within 24-36 hours of life. The newborns will be separated into two groups of ten each and will serve as their own controls. The first group will wear Probe Cover A. The second group will wear Probe Cover B. Probe covers will be removed on the third day of wear. Probe covers and the skin under the probe will be swabbed for bacterial growth. An exposed patch of skin opposite from the probe cover will be swabbed as a background (control) check of skin bacteria. Culture swabs will be placed in saline and serial dilutions will be made before plating onto sheep blood agar (SBA) and mannitol salt agar (MSA) plates for detection and enumeration of skin flora. Significant differences in bacterial types and amount will be noted between exposed skin and the two types of probe-covered sites. The basic parametric procedure for testing differences in groups is the t-test. The paired t-test will compare results from skin under Probe Cover A with uncovered and skin under Probe Cover B. The Mann-Whitney-U test will be used to test the difference between the two independent samples.

**Progress:** Fifteen subjects were entered in FY 97 for a total of 20 who completed the study. Data analysis is in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/190		<b>Status:</b> On-going	
<b>Title:</b> The Effects of Thermocouple Sensor Placement on Neonatal Skin Temperature Measurement					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Lori A. Loan, MSN, RNC					
<b>Associate Investigators:</b>		Lauran T. Taquino, RN, MS			
Susan T. Blackburn, Ph.D., RN, FAAN		Karen A. Thomas, Ph.D., RN			
<b>Key Words:</b> Skin temperature, neonatal, thermocouple sensor placement					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		05/16/97	

**Study Objective:** The objectives of this study are to compare temperature readings from probes placed on peripheral skin sites with readings of axilla temperature, and to compare temperature readings from probes placed on the abdomen and back during periods when the infant is lying -on and not lying-on the temperature probes. Also, to evaluate the effects of body size on accuracy of temperature probe measurements from selected sites, and when the infant is lying-on versus not lying-on the probe.

**Technical Approach:** This descriptive study is designed to objectively evaluate several common nursing practices and beliefs regarding the care of neonates and the placement of temperature probes. The study seek to provide a physiologic basis to support and validate nursing practice. Four body sites will be studied simultaneously through the use of a small thermocouple sensor and two channel continuous readout device. Data will be collected for one hour with the subject in each of two common positions, supine and prone. Environmental temperature and basic demographic data will also be collected for each subject and study period. The study period will consist of approximately 2.5 hours for each study subject and will not interfere with or alter the standard neonatal nursing and medical care of that infant. This study is sponsored by the local chapter of the national professional association for neonatal nursing and is designated to support data collection in multiple hospital sites. Data from all sites will be aggregated for the purpose of analysis and reporting. Descriptive statistics will be use initially to examine differences in temperature readings from the four sensors. Further analysis will examine clinically and statistically significant changes in temperature between the four sites and between lying-on and not lying-on the sensors. comparisons will also be made of differences in temperature values between sites and between infants of different weight groups.

**Progress:** No subjects were entered during FY 97, 12 have been entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/137		<b>Status:</b> On-going
<b>Title:</b> Single Woman's Breast Cancer Program				
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jun 98	
<b>Department:</b> Nursing			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> Lori A. Loan, MSN, RNC				
<b>Associate Investigators:</b>			Nancy F. Woods, Ph.D., RN	
<b>Key Words:</b> Cancer:breast, single women				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
			<b>Periodic Review:</b> 9/30/97	

**Study Objective:** There are five study purposes: to (1) test the effectiveness of a home-based counseling intervention for single women with early stage breast cancer with dependent children; (2) investigate the causal model underlying the intervention; (3) explore time related patterns of change in individual study participants; (4) develop a discriminant function that effectively categorizes women and children most able to benefit from the intervention; and (5) test the cost-effectiveness of the intervention. The goal of the intervention is to improve psychosocial adjustment and quality of life in single women with early stage breast cancer and their dependent children.

**Technical Approach:** This study will enroll 200 single females who have a recent diagnosis (11 months or less) of early-stage breast cancer (Stage 0, 1 or 2). Subjects will be inpatients or outpatients, from medical, surgical or radiation oncology departments. Subjects will be randomized prior to initial contact so that the woman is invited to participate in either the coached or evaluation group. When subjects have agreed to participate, an in-home appointment is made with the evaluation nurse. Consent is obtained on the first visit and questionnaires are administered. Child participation is desirable but not mandatory. Initial explanation to the child is always left to the mother, but the nurse will provide additional information and obtain written consent from the child, if willing. All families receive 4 evaluation visits. Women randomized to the coached group receive an additional 5 in-home visits by the coach. At the end of the study, all women receive thank you a letter and those who were randomized to the evaluation group receive \$20 for each visit and an informational packet about breast cancer. Data will be analyzed by 5 major methods: formal statistical tests of the effect of the intervention (MANCOVA); investigation of the explanatory model underlying the intervention (structural equation modeling); exploration of time-related patterns of change in individuals (trend analysis and latent growth model); discriminant analysis and cost-effectiveness analysis. All of these data analytic components constitute outcome analyses and there will also be a process evaluation component.

**Progress:** No subjects were entered during FY 97 from MAMC, 79 subjects have been entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/076		<b>Status:</b> On-going	
<b>Title:</b> Gastric/Jejunal Feeding: Nutritional Outcomes and Pneumonia					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mary S. McCarthy, AN					
<b>Associate Investigators:</b> CPT Kurt W. A. Grathwohl, MC MAJ Susanne J. Clark, AN			MAJ Bernard J. Roth, MC 1LT Faith U. Watanabe, SP		
<b>Key Words:</b> Feeding:gastric, Feeding:jejunal, pneumonia					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 05/16/97

**Study Objective:** 1) To compare nutritional outcome between patients randomized to gastric or jejunal tube feeders as measured by: a) daily caloric intake, b) subjective global assessment, c) biochemical parameters, d) delayed cutaneous tests and e) indirect calorimetry. 2) To compare rates of nosocomial pneumonia between gastric and jejunal fed patients as measured by: a) new & persistent infiltrate on chest x-ray (CXR), b) fever, c) sputum culture, d) leukocytosis, and e) bronchoscopically directed protected specimen brush. 3) To compare colonization rates between a subset of gastric and jejunal fed patients, at three sites (oropharynx, trachea, stomach); specific focus being Gram-negative bacilli, as measured by quantitative and qualitative microbiology analysis.

**Technical Approach:** This proposed study is a replication of a prior study done by Montecalvo et al. (Appendix A) in the medical model. Areas of interest include modifiable and non-modifiable person factors, social and physical environmental factors, physiological factors, pathophysiological factors, behavioral factors, symptoms, cognitions/emotions, and drives/sensations. Infants who are prescribed a feeding tube in one of two places, the stomach or the small intestine. Both methods are commonly used in this hospital. If you are to receive tube feedings in the stomach your doctor will pass a soft, flexible tube down your nose or mouth into your stomach. If you are to receive tube feedings in the small intestine, a radiologist will pass a soft, flexible tube down your nose or mouth using a lighted scope to guide the tube placement into your small intestine. It is the policy of this hospital to confirm the placement of the tube by xray before feedings can begin. This is ordered by the physician and will be performed whether or not you participate in this study. Shortly after having the tube in place, the principal investigator or the project director will conduct a noninvasive metabolic test at the bedside to estimate your calorie needs for tube feeding. This test measures the amount of energy you use while you are ill in the ICU. It will be performed each week. In addition, specimens of blood, urine, sputum and stomach contents will be obtained to evaluate your nutritional status and monitor for infection or bleeding. Lastly, your health record will be examined by the investigator or the project director for the following information: pertinent medical history, admission vital signs, current medications, height and weight, and tube feeding regimen.

**Progress:** 22 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/128		<b>Status:</b> Terminated	
<b>Title:</b> Natural Killer Cell Activation in Women with Early Stage Breast Cancer					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> May 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Thomas H. Miller, AN					
<b>Associate Investigators:</b>			Betty J. Gallucci, Ph.D., RN		
<b>Key Words:</b> Cancer:breast, killer cell activation					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97	

**Study Objective:** To obtain preliminary data for the Research Proposal entitled "Natural Killer Cell Activation in Women with Early Stage Breast Cancer" to be submitted for the DOD Breast Cancer Research Initiative July 15, 1996. The major critique of the same proposal, which was submitted in September 1995, was that no preliminary data was available.

**Technical Approach:** For this preliminary study, 10-20 female subjects will be recruited from those patients obtaining a breast biopsy at MAMC or volunteers recruited by advertisement. Those patients interested will be advised to contact the researchers and be screened for inclusion/exclusion criteria. The women will have blood drawn for testing at the University of Washington School of Nursing Laboratory. Sixty to 100 ml of venous blood will be collected into heparinized vacuum tubes. Appropriate cells will be separated and tested for NK cell cytotoxicity and activation antigen expression. Students t-test and a two-way analysis of variance for repeated measures will be used to detect difference in the mean activation antigen expression before and after IL-2 incubation.

**Progress:** This protocol was terminated because it did not receive grant funding. No patients were entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/066		<b>Status:</b> Suspended	
<b>Title:</b> Postpartum Physical Fitness in Military Women					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Sep 00		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Elizabeth A. Mittelstaedt, AN					
<b>Associate Investigators:</b> Lori A. Loan, MSN, RNC M.G. Millien			Debra DePaul, RN Elizabeth Pulos, Ph.D.		
<b>Key Words:</b> Physical fitness, postpartum, military women					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** 1). Describe the physical fitness of postpartum active duty military women during the first nine months (i.e., at 6 weeks, 6 months, and 9 months postpartum) following childbirth as compared to non-postpartum female soldiers. 2) Describe the health promotion behaviors (specifically exercise, diet, sleep and smoking) used by pregnant/postpartum active duty military women during pregnancy and in the first nine months following childbirth (i.e., pre-pregnancy, at 34 weeks pregnant, 2 weeks postpartum, 6 weeks postpartum, 3, 6, and 9 months postpartum) as compared to non-postpartum female soldiers. 3) Examine the extent to which health promoting behaviors (specifically exercise, diet, sleep and smoking) facilitate physical fitness in postpartum and non-postpartum female soldiers.

**Technical Approach:** The study will utilize a prospective, longitudinal, panel design with a two-group comparison. APFT and American College of Sports Medicine physical fitness measures and health promoting behaviors (exercise, sleep, and smoking) data will be analyzed from pregnant/postpartum (n = 80) and non-pregnant soldiers (n = 80) assigned to Fort Lewis, Washington. Data will be collected from in-person and phone interviews, daily health behaviors' recall and record review. Data will be analyzed using descriptive statistics, Chi-square, independent t-test, Pearson product-moment correlation coefficient and RM-ANOVA.

**Progress:** The grant for this protocol was not funded. The investigators are in the process of resubmitting with revisions. Therefore, the protocol has been put in a suspended status.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/082		<b>Status:</b> Completed	
<b>Title:</b> Deployment Competency and Skill Retention of Anesthesia Care Providers Using the Field Anesthesia Machine					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Connie J. Moore, AN					
<b>Associate Investigators:</b> CPT Evelyn J. Williams, AN			CPT Nancy L. Sweet, AN		
<b>Key Words:</b> Field Anesthesia, anesthesia care provider, experience, skill level					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97	

**Study Objective:** 1) To determine how anesthesia care providers (ACPs) experience correlates with accurate delivery of a volatile anesthetic while using the field anesthetic machine; and 2) to determine what level of skill retention occurs at four weeks and four months post-training.

**Technical Approach:** This study will obtain its sample from all active duty and reserve component ACPs. The sample will be at least 46 ACPs. The researchers will outline the study procedure to ACPs during an anesthesia department staff meeting. Each ACP will complete a detailed demographic sheet designed to obtain experience information. In this group setting, researchers will instruct each participant to calculate the correct carrier flow to deliver a certain percentage of isoflurane, first by using arithmetic calculations and then by manipulating a circular slide rule commonly used for this calculation. The results of these calculations will be recorded as data. then, the researchers will request that each participant correctly operate the FAM in order to deliver the prescribed isoflurane percentage. Correct or incorrect manipulation of the FAM will be recorded as data. For the first 20 participants, didactic and demonstrative training on all tested areas will then occur, with an immediate post-test. This post-test will be identical to the pretest, except for the isoflurane concentration. Retesting at four weeks and four months will repeat the post-test. Data analysis will utilize the Mann Whitney U test, with  $p < 0.05$  for significance, to analyze the question: How does ACP experience correlate with accurate delivery of volatile anesthetic agents while using the FAM? A Student's t-test, with  $p < 0.05$  for significance, will be used to analyze the question: What level of skill retention occurs at four weeks and four months post-training?

**Progress:** A convenience sample of 20 military anesthesia providers was obtained. Due to attrition, a final sample of 11 completed all aspects of the study. Using a Spearman rank correlation statistic, accurate delivery of an anesthetic did not significantly correlate with any of the predictor variables ( $p > .05$ ). Using the Friedman test, no significant difference in calculation or demonstration scores was found among the three times of testing posttest, retest at 4 week, and retest at 4 months.

A lack of significant correlation between experience and performance was noted in this study. Also, no significant loss of original performance occurred through the 4 month testing point. Any change in practice related to these findings would require a larger sample size in a similar study.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/015		<b>Status:</b> Completed
<b>Title:</b> Social Support of Women Treated for Breast Cancer				
<b>Start Date:</b> 11/15/96		<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Penny M. Moureau, AN				
<b>Associate Investigators:</b>		Banner HM		
<b>Key Words:</b> Cancer:breast, social support				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** To ascertain if the level of social support differs with passage of time in women treated for breast cancer.

**Technical Approach:** This descriptive, comparative survey will determine if there is a relationship between the level of social support and the passage of time and determine what differences (if any) exist in the levels of that support at the beginning of treatment and after 3 months of treatment in women with breast cancer.

**Progress:** Forty-nine subjects were studied. The information was used to complete the principal investigator's master's thesis. Although there was no change in levels of social support three months into treatment for breast cancer, it is recommended that nurses stringently assess women for social support and fortify support when needed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/106		<b>Status:</b> On-going	
<b>Title:</b> Natural Killer Cell Activation and Apoptosis in Women with Early Stage Breast Cancer: Potential Measure for Nursing Research					
<b>Start Date:</b> 06/20/97			<b>Est. Completion Date:</b> Apr 98		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Penny M. Moureau, AN					
<b>Associate Investigators:</b> LTC Thomas H. Miller, AN			Betty J. Gallucci, Ph.D., RN Genevieve M. Fuller		
<b>Key Words:</b> Cancer:breast, Natural Killer Cell Activation					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0		<b>OMA Cost:</b> \$0.00		9/30/97	

**Study Objective:** 1) To explore the whole blood assay for the measurement of activation antigens on natural killer (NK) cells. 2) For our laboratory to select and gain experience with a measure of apoptosis or programmed cell death. 3) Describe and compare expression of NK cell activation antigens in women with hyperplasia and early stage breast cancer and women without breast disease, prior to and after IL-2 incubation. Expression of activation antigens is not normally detected in peripheral NK cells of healthy women, but is present in such illness states as chronic fatigue syndrome (40) and is also present after incubation with IL-2. 4) Explore the potential mechanisms for depression of NK cell cytotoxicity seen in women with breast cancer by determining the percent of apoptotic cells across all groups of women after activation by IL-2.

**Technical Approach:** NK cells play an important role in immune surveillance against tumor cells and are the first line of resistance against infections. NK cell activity is increased in individuals with healthy lifestyles and is depressed in individuals who experience acute or chronic stressors of disease symptomatology such as breast cancer. Activation of NK cells leads to the expression of activation antigens on the cell surface, initiates production of cytokines, increases levels of cytotoxicity, and promotes programmed cell death. The methodologic aims of our study are to gain experience in the laboratory with the whole blood assay for activation antigens and to determine which of the apoptosis assays will be the most rapid, reliable and sensitive. For nurse researchers, measurement of natural killer cell activation has the potential to monitor an immunologic outcome of primary and tertiary prevention strategies for breast cancer.

**Progress:** Study has not started because some changes are being made to the questionnaire such as omit breast cancer risk questionnaire, change # of tubes of blood needed from 10 to 4-6. Changes are still pending IRB approval.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 93/115		<b>Status:</b> Completed	
<b>Title:</b> Neonatal Outcomes in a Modified NICU Environment					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Michelle T. Renaud, AN					
<b>Associate Investigators:</b> Susan T. Blackburn, Ph.D., RN, FAAN			LTC Joanna C. Beachy, MC Karen A. Thomas, Ph.D., RN		
<b>Key Words:</b> Neonates, modified NICU					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 05/16/97

**Study Objective:** (1) To evaluate the effects of a modified NICU environment on physiological and neurobehavioral parameters in two groups of preterm infants and in high risk full term infants during hospitalization and post discharge; (2) to evaluate the effects of a modified NICU environment on infant-caregiver synchrony and stressors in the period of transition from hospital to home, and post-discharge.

**Technical Approach:** This is a continuation project of an ongoing study. This project extends longitudinal follow-up through the addition of a home visit and incorporates parent behavioral responses as factors relevant to infant outcomes. At the Post-Discharge Clinic Visit, 2 - 3 weeks following discharge, the mother will be asked to complete the Transition from NICU to Home Questionnaire during the infant's regularly scheduled follow-up visit. The home visit will be scheduled at the parents convenience at 82 weeks post discharge. At the home visit, the infant's neurobehavioral status will be assessed using the Brazelton Newborn Assessment Scale (BNBNS) and the infant's sleep-wake pattern will be recorded using the Newborn Child Assessment Sleep Activity (NCASA) record. Parents will complete the Parenting Stress Index (PSI) during the home visit. Parent-infant interaction during a feeding will be observed using the Nursing Child Assessment Feeding Schedule (NCASF). Home visits will be arranged to accommodate the feeding schedule.

ANOVA and repeated measures ANOVA will be used to test group differences in the BNBAS, NCASF, PSI and Transition from NICU to Home Questionnaire. The 24-hour recordings of sleep obtained by the NCASA will be summarized and differences in total sleep and wake time, number of awakenings, and synchrony to day-night pattern will be tested using ANOVA and repeated measures ANOVA. Cyclicity of NCASA data will be determined within subject using cosinor analysis.

**Progress:** 126 infants were randomized as described in the protocol; 112 subjects completed the study. Results show that the high risk infants cared for in the modified environment had more night sleep, less crying, and less night feedings. This was also true at two months after hospital discharge. Few statistically significant neonatal physiologic and neurobehavioral outcomes were found. However, the experimental infants transitioned sooner to nipple feedings, had shorter overall stays, demonstrated more night sleep, and had less nighttime crying. No difference in infant-caregiver synchrony and stressors in the period of transition from hospital to home was observed between experimental and control infants. This study demonstrates some improvement of neonatal outcomes in a modified environment, but the small sample size limits the findings.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/101	<b>Status:</b> Completed
<b>Title:</b> Fatigue Following Childbirth: Military Family Outcomes		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Michelle T. Renaud, AN		
<b>Associate Investigators:</b>		
Marcia G. Killien, Ph.D.	Debra DePaul, RN	
Karen A. Thomas, Ph.D., RN	Susan T. Blackburn, Ph.D., RN, FAAN	
LTC Michelle T. Renaud, AN	Lori A. Loan, MSN, RNC	
Lorna R. Imbruglio, BSN, MSN	Jeanette Zaichkin, BSN	
Martha J. Lentz, BSN, MN, Ph.D.	Sue E. Chambers, RN	
	Julianna Ellis	
<b>Key Words:</b> childbirth:fatigue, childbirth:military		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/16/97

**Study Objective:** To determine if an advanced practice nursing intervention to reduce fatigue will promote job well-being, parenting ability, and infant outcomes among military active duty personnel and their spouses/partners following the birth of an infant.

**Technical Approach:** Pregnant females and their spouses/partners (if applicable) will be recruited during weeks 28-32 of gestation in the prenatal clinic at MAMC. Data will be collected at six time points: prenatally at time of enrollment and post birth when the infant is 24-48 hours, 2 weeks, 2 months, 4 months, 6 months or age. Time measures correspond to typical timing of clinic visits. During the clinic visit, parents will complete a packet of questionnaires specific to each time of measure and active military status. If only one parent attends the clinic visit, the other parent will complete their part of the questionnaire packet at home and return it by mail. Following birth, infant neurobehavioral status will be assessed by trained study personnel at 24-48 hours of age. At 4 & 6 months of age parent-infant interaction will be assessed during the clinic visit using the NCATS observational tool. At 6 months of age infant development will be assessed by trained study personnel using the CAT/CLAMS-r and Denver II assessment instruments. Experimental subjects will begin the fatigue modulating intervention following the initial assessment at Time 1. Throughout the study experimental subjects will receive care from the project's advanced nurse practitioners. Continuous monitoring of the intervention's integrity and effectiveness will allow the nurse practitioner to reinforce and modify the intervention as appropriate.

**Progress:** A total of 392 subjects were entered in the study. T tests and chi square analysis revealed the experimental and control groups to be comparable with respect to demographic and psychosocial measures before initiation of the intervention. T-tests revealed significant differences at 2 months postpartum between the experimental mothers' total sleep and longest bout of nighttime sleep and the control mothers. Experimental infants had significantly fewer bouts and longer nighttime bouts than controls. At 4 months postpartum, experimental mothers continued to have significantly longer nighttime bouts of sleep as well as experimental infants. There were no significant differences between the groups in fatigue, military job satisfaction, military job absenteeism and retention, exercise, parent/infant interaction, or infant developmental concerns. This fatigue-reducing intervention appears to be effective in promoting sleep time and sleep consolidation in mothers and infants, especially at two months postpartum. However, it does not appear to decrease parents' perception of fatigue, parenting ability, or job well-being.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/148		<b>Status:</b> Completed
<b>Title:</b> Feasibility and Patient Satisfaction with Wearing an Eye Mask and Ear Plugs During Regular Sleep Times While in the Coronary Care Unit				
<b>Start Date:</b> 08/16/96		<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Mary E. Riley, AN				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Sleep, CCU, eye mask, ear plugs				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** The purpose of this study is to describe the feasibility and patient satisfaction with wearing an eye mask and ear plugs during the person's regular sleeping time while in an Intensive Care Unit (ICU).

**Technical Approach:** Subjects for this study will include all ICU admissions except for those patients either undergoing cardiac admissions or who are currently involved in another study. A minimum of 30 subjects will be used for the study. A fourteen-item questionnaire will be administered every morning for up to three consecutive days during their ICU stay. The subjects will be asked their level of satisfaction with the use of the eye masks and ear plugs and also their overall ICU experience. Descriptive statistics will be used to describe and summarize results obtained from the questionnaires. The means, frequencies, and percentages of scores for each item on the questionnaire will be calculated. Demographic data will be displayed in a table with the calculated means, standard deviations, modes, and medians as appropriate.

**Progress:** Eighteen subjects were studied. In general, the use of the eye mask was found to be feasible and should be considered as a viable intervention for further testing to determine its effect on optimal sleep in the ICU patient.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/079		<b>Status:</b> Completed	
<b>Title:</b> Soldier HIV Behavior Modification					
<b>Start Date:</b> 02/17/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Catherine M. Schempp, MC					
<b>Associate Investigators:</b> Debra Pontius			Ann E. Hyder LTC Roberta E. Dyer		
<b>Key Words:</b> HIV, behavior					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 05/16/97

**Study Objective:** 1) What is the current knowledge level concerning HIV and AIDS within the units, and does knowledge level change after the intervention? 2) What are the current beliefs toward HIV and AIDS, and risk behaviors regarding sexual practices, within the units and do beliefs and risk behaviors change after the intervention? 3) At the unit level is a peer led HIV education program more effective than the current nurse led HIV education program at increasing adaptive intentions and attitudes toward safe sex practices? These aims will be addressed utilizing the Health Belief Model as the theoretical framework.

**Technical Approach:** The purpose of this study is to determine if the use of a peer leader as opposed to the HIV nurse or the size of the group receiving the intervention makes any change in the outcome measures of knowledge of HIV and AIDS, beliefs toward HIV and AIDS, and risk behaviors. The theoretical model for this proposal is the Health Belief Model. The design of the study will include four groups receiving the intervention and a control group. The units requesting HIV education classes will be assigned to either a large or small group depending on the size of the unit and will receive the intervention from either the peer leader or the HIV nurse. This study will involve approximately 35 units with approximately 1700 soldiers. The units will be further stratified by their mission to allow for differences based on individual requirements to meet the unit mission. The control group will consist of units that do not request HIV education classes during the intervention period. The research questions will be analyzed using analysis of variance upon the data gathered from three questionnaires, and post hoc tests will be performed on significant differences. The first questionnaire will be administered prior to the intervention and will consist of a comprehensive assessment of knowledge, beliefs and risk behaviors. The second questionnaire will be administered immediately after the intervention and will focus on knowledge. The third questionnaire will be administered after three months and will focus on beliefs and risk behavior.

**Progress:** Approximately 2300 subjects were studied. All data have been collected and data analysis is in progress.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/079		<b>Status:</b> Completed	
<b>Title:</b> Determination of Key Events in Female Military Adolescents' Lives Which May Predispose Them to Depressive Episodes					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Feb 98		
<b>Department:</b> Nursing			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Lisa L. Spence					
<b>Associate Investigators:</b>			Lori A. Loan, MSN, RNC		
<b>Key Words:</b> Adolescents:military, depression					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To attempt to identify key events in female adolescent's lives which may predispose them to depressive episodes.

**Technical Approach:** The investigator will conduct two focus groups, each composed of five female adolescent volunteers. The small focus group size is to promote discussion and decrease intimidation among study participants. The volunteers will be obtained by placing flyers in the Adolescent Clinic at Madigan Army Medical Center. Once the potential subjects respond to the flyers, the investigator will give them more information via telephone. If the potential subject is less than 18 years old, the investigator will speak with the subject's parent first. Once the parent has been presented with the study information, the parent will be asked if it is all right to speak with her daughter. The focus groups will be conducted during the months of February through April, 1997, at a time and place mutually agreed upon by the volunteers and the investigator. The focus group sessions will be recorded via audiotape. During each of the two focus groups, a brief discussion regarding methods of coping with stress will be provided, as well as an educational handout on the same topic. If the investigator should discover that a volunteer is suicidal, a protocol will be followed. The protocol was devised by the investigator after consultation with Dr. Martinko, M.D., Chief, Adolescent Clinic, Madigan Army Medical Center. Dr. Martinko has also reviewed the finished protocol. Refer to the attached Protocol for Mental Health Referral of Study Participants. Once the focus groups are completed, the audiotapes will be transcribed. During transcription of the audiotapes, any recorded names will be omitted. The data will then be analyzed using the computer software package Ethnograph. The results of the study will be documented in the investigator's final written Master's project. An abstract of the results will be provided to Madigan Army Medical Center.

**Progress:** Six female adolescent military dependents were studied. While the actual data cannot be generalized due to the small samples size, their responses are still thought-provoking. All of the teens in the focus group seemed acutely aware of the meaning of depression and of times in their lives when they experienced depressive feelings. Some of the key depressive events identified by the teens include parental divorce, father's absence due to military deployment, death of a boyfriend, leaving friends behind when moving, and having a father fight in the Gulf war. The female adolescents were able to generate a few solutions to the pressing situations. One solution was to have a military family with teenage dependents sponsor an incoming family with teenage dependents. They also suggested that a teen recreation center be provided on a military base to provide teens with a place to "hang-out" and meet new friends. In general the results of this pilot study seem to indicate that the focus group format and the developed focus group materials are appropriate for use with female adolescents and for the purpose of the study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/010		<b>Status:</b> Completed
<b>Title:</b> Impact of a Research Project on Clinical Practice: Year Three Evaluation				
<b>Start Date:</b> 11/15/96		<b>Est. Completion Date:</b> Sep 97		
<b>Department:</b> Nursing		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Suzanne K. Wilson, MSN, RN				
<b>Associate Investigators:</b>		MAJ Pamela S. Birgenheier, AN		
<b>Key Words:</b> Clinical practice, research				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** The objective of this study is to evaluate the effect of one unit's participation in a multi-site standard of practice research utilization project on clinical practice three years later.

**Technical Approach:** The study plans to use the data that were used for a unit level QA chart audit [preterm infants admitted to the NICU and transitioned to an open crib between 1 January 1995 - 15 October 1995] to describe the current method or standard of practice of transitioning infants to an open crib. To evaluate the unit's method or standard of practice of transitioning infants to an open crib prior to the 1992 project, a chart audit of infants admitted to the NICU requiring incubator support and transitioned from an incubator to an open crib between 1 February 1991 and 30 January 1992 will be conducted to serve as a historical documented basis of the unit's method or standard of practice of transitioning infants to an open crib. A comparison of the pre- and post-project's findings will be made in order to determine if the project's findings will be made in order to determine if the projects findings were utilized by the nurses.

For this study, indicators of successful research utilization of project's findings are: (1) staff assimilation of the transition to the open crib protocol findings as the standard of practice (SOP) and (2) documented entries of the use of the project's findings [(a) such as early insulation of infant in a sleeper; (b) incubator on manual control temperature and decreased to 28o C before the infant is moved to an open crib; and (c) the actual move to the open crib] will be observed in the patient chart. In addition socio-demographic characteristics will be described.

The data collection period will consist of the transcription of study's attributes from the retrospective 1995 NICU QA data sheet and the retrospective 1991/1992 NICU chart audit data to the study's data collection sheet. Descriptive statistics and Chi-square/ANOVA will be determined.

**Progress:** Results from all 16 Group B eligible preterm infants' charts indicate that the nurses, regardless of when assigned to the unit, adopted the transition research project findings as standard of practice as evidenced by the chart reviews. Based on these positive results, unit participation in research projects may be considered more favorably in the future as a method to update clinical practice.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF  
OBSTETRICS/GYNECOLOGY**

# Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/136		<b>Status:</b> Completed	
<b>Title:</b> Teen Pregnancy					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Byron C. Calhoun, MC					
<b>Associate Investigators:</b> CAPT Anne McEwen, MC			MAJ Nathan J. Hoeldtke, MC		
<b>Key Words:</b> Pregnancy, teen, special clinic					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To demonstrate that unique and comprehensive teen clinics in the military provide improved outcomes.

**Technical Approach:** Pregnancy in teens remains a conundrum. Various studies provide confusing results regarding comprehensive clinics and pregnancy outcomes. Our study seeks to expand the investigation into teen pregnancy by providing a platform of a comprehensive clinic compared to married teenagers in routine obstetrical clinics in a cohort of single women between the ages of 20-24 years. We believe that we will find an improved outcome in the teenagers in the focused clinic. Demographic data including age, race, gravidity/parity, tobacco use, and substance abuse will be analyzed. Outcome will be examined utilizing week gestation at delivery, fetal birth weights, APGARS, anemia, NICU admission days, deliveries < 2500 gms, mode of delivery, intrauterine growth delay, c-section rates, preeclampsia, gestational diabetics, large for gestational age (>4000 gms), deliveries after 42 weeks, and delivery complications (i.e., postpartum hemorrhage, chorioamnionitis). Retrospective chart review will be used to compare the cohorts. Descriptive statistics, as well as multivariate analysis, will be used to examine the data.

**Progress:** Approximately 600 patients were entered in this study. Statistical analysis was done using chi square with Pearson's correlation and analysis of variance was performed on Statview Statistical Package with  $p < 0.05$  as significant. Statistical differences were noted in the mean delivery weights ( $p < .05$ ), preeclampsia ( $p < .04$ ), gestational diabetes ( $p < .01$ ), history of substance abuse ( $p < .0001$ ), and tobacco use ( $p < .0001$ ). None were clinically significant. The focused, adolescent obstetrical clinic appears to provide perinatal morbidities equal to the low-risk population, generating better than expected outcomes for pregnant teenagers.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/108		<b>Status:</b> On-going	
<b>Title:</b> Transanal Ultrasonography (TAUS) in the Repair of Episiotomy Anal Sphincteroplasty					
<b>Start Date:</b> 06/20/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary D. Davis, MC					
<b>Associate Investigators:</b>			CPT Jerome L. Buller, MC		
LTC Milo L. Hibbert, MC			COL Lawrence A. Decker, MC		
McClure G			LTC Frederick B. Brown, MC		
COL Romeo P. Perez, MC			LTC Richard A. Sherman, MS		
<b>Key Words:</b> Anal sphincteroplasty, episiotomy, ultrasonography					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** To assess the efficiency of intra-operative transanal ultrasound (TAUS) in the repair of the anal sphincter at episiotomy.

**Technical Approach:** Transanal ultrasonography (TAUS) has proven to be an effective means of assessing the structure and function of both the internal and external anal sphincters. Preliminary studies at Madigan Army Medical Center have shown that the intra-operative use of TAUS provides rapid and precise identification of both the internal and external anal sphincters, as well as immediate assessment of sphincter continuity and the success of sphincteroplasty. We propose to determine if the intra-operative use of TAUS will improve the anatomical and functional outcome of (a) episiotomy repair and (b) sphincteroplasty. (a) One hundred obstetric subjects at 28 weeks gestation or greater will be evaluated by endoanal ultrasound, pudendal nerve velocity and anal manometry to obtain initial. Episiotomies will be rendered only if obstetrically indicated. Those subjects requiring episiotomies at delivery will be randomly assigned to one of two groups. Those who will receive TAUS, and those who will not receive TAUS for episiotomy repair if episiotomy is indicated at delivery. Those subjects not requiring episiotomy will be dropped from the study. (b) In addition, twenty gynecologic subjects scheduled to undergo and sphincteroplasty will receive identical pre-operative evaluations of anal manometry, pudendal nerve velocities and endoanal ultrasonography to establish pre-operative values. They will be randomly assigned to one of two groups, those having repair with the aid of TAUS, and those undergoing sphincteroplasty without the aid of TAUS. All subjects (both obstetric and gynecologic) will be evaluated six weeks after surgery with repeat and manometry, pudendal nerve velocity and endoanal ultrasound. Pudendal nerve velocities, internal and external and sphincter length and width, manometric pressures, and pelvic organ prolapse quantification (POPQ) scores will be compared.

**Progress:** 20 subjects were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/107	<b>Status:</b> On-going
<b>Title:</b> The Effectiveness of Mechanical Devices in the Prevention of Exercise Induced Urinary Incontinence in the Female Soldier		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Nov 97	
<b>Department:</b> Obstetrics/Gynecology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Gary D. Davis, MC		
<b>Associate Investigators:</b>		
LTC Milo L. Hibbert, MC	CPT Jerome L. Buller, MC	
COL Romeo P. Perez, MC	COL Lawrence A. Decker, MC	
	LTC Richard A. Sherman, MS	
<b>Key Words:</b> Urinary incontinence, exercise induced, mechanical devices		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To determine the effectiveness of mechanical devices in the prevention of exercise induced incontinence in the female soldier.

Technical Approach: Our recent study of urinary incontinence among female soldiers revealed that 30 percent use precautions of various types to help prevent urinary incontinence in the field or during exercise. We propose to study the effectiveness of four types of mechanical devices for the prevention of urinary incontinence in female soldiers by comparing perineal pad weights after exercise with and without the mechanical devices. Multichannel urodynamic parameters will also be compared with and without the mechanical devices in place. This will objectively document the effectiveness of each device in the treatment of urinary incontinence during exercise.

Progress: Study has not started; pending arrival of mechanical devices.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/129		<b>Status:</b> On-going	
<b>Title:</b> The Non-invasive Detection and Characterization of Anal Incontinence in the Parous Female Population					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary D. Davis, MC					
<b>Associate Investigators:</b> CPT Clinton S. Beverly, MC			LTC Bradley G. Bute, MC LTC Phillip L. Mallory II, MC		
<b>Key Words:</b> Incontinence:anal, pregnancy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** This study attempts to determine the frequency and nature of obstetric-related anal incontinence by using non-invasive techniques. Anal sphincter and pudendal nerve status would be assessed and correlated with patient questionnaire complaints and manometric measurement of function.

**Technical Approach:** Permanent anal incontinence is reported to complicate 4-6 percent of vaginal deliveries and has been blamed on pudendal nerve injury or sphincter muscle damage. A non-invasive study of 300 pregnant women during and after pregnancy is proposed to attempt to differentiate between neuronal, muscular or combination injuries which produce incontinence. Volunteer subjects would be assessed for: pudendal nerve terminal motor latency as a measure of innervation, manometric variables as an indicator of function and transanal ultrasound as a morphologic study. Comparison of results before and after delivery would help determine the cause of obstetric-related anal incontinence. Standardized anorectal physiology data would be recorded for each patient to include resting pressure, maximal squeeze pressure, presence of rectoanoinhibitory reflex, sphincter length, and sensory threshold. Statistical analysis will evaluate for differences being due to chance with less than five percent being considered significant ( $p \leq 0.05$ ). Tests for ordinate and continuous variables will be employed as appropriate.

**Progress:** 62 subjects were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/038		<b>Status:</b> Completed	
<b>Title:</b> Ambulatory Recording of Urodynamic Functioning in Female Soldiers During Training					
<b>Start Date:</b> 12/15/95			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary D. Davis, MC					
<b>Associate Investigators:</b> LTC Richard A. Sherman, MS			CPT Lynda S. Gilliam, MC		
<b>Key Words:</b> Incontinence, female soldiers, computer aided measurement system					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** To determine whether ambulatory urodynamic recordings from female soldier's participating in the actual situations which elicit urinary incontinence will: (1) show that (A) some female soldiers undergoing the rigors of airborne training will demonstrate urodynamic changes as well as physical findings when urinary incontinence develops or progress, (2) show that female soldiers who complain of incontinence, but demonstrate no abnormalities on laboratory urodynamic testing will demonstrate ambulatory urodynamic abnormalities when performing the activities they report as eliciting the incontinence, (3) demonstrate different patterns of ambulatory urodynamic abnormalities when compared to similar female soldiers who complain of incontinence but demonstrate abnormalities in the standard urodynamic laboratory, and in comparison to continent female soldiers, and (d) show that incontinent female soldiers who only demonstrate ambulatory urodynamic abnormalities will show different patterns before and after successful treatment for urinary incontinence.

**Technical Approach:** 100 female soldiers will be recruited by questionnaire or from clinic. We will perform ambulatory recordings to (1) compare urodynamic patterns of normal and incontinent female soldiers, (2) to compare urodynamic patterns of incontinent female soldiers before and after successful treatment, and (3) review ambulatory recordings of incontinent female soldiers who do not demonstrate incontinence in the laboratory urodynamic setting.

**Progress:** Fifty subjects with exercise-induced urinary incontinence were recorded during both stationary and ambulatory tests. Ten controls were also studied.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/084		<b>Status:</b> Terminated	
<b>Title:</b> Incidence of Exercise Related Musculoskeletal Injuries vs Phase of the Menstrual Cycle					
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Gary D. Davis, MC					
<b>Associate Investigators:</b> LTC Richard A. Sherman, MS			LTC D. E. Casey Jones, MC Lilliam L		
<b>Key Words:</b> Musculoskeletal injury, exercise, menstrual cycle					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To determine the relationship between exercise related musculoskeletal injuries and the phase of the menstrual cycle.

**Technical Approach:** An unanticipated finding of our studies on urinary incontinence among female soldiers supported by the Defense Women's Health Research Program was that the incidence is much worse and more prevalent during the luteal phase of the menstrual cycle. At least one civilian study has found that more women are injured while playing soccer during the luteal phase. There is some evidence that ligaments are stretched more during this phase possibly due to the presence of more progesterone. If ligaments are actually being significantly stretched/weakened during this phase, a disproportionate rate of exercise related injuries would occur during the luteal phase. We propose to determine whether this relationship exists to an important extent by asking all female soldiers who sustain exercise related musculoskeletal injuries at Fort Lewis how long it has been since their last period to determine where they are in their cycles. The subjects will also have their blood drawn the morning after the injury and once again during the follicular phase of their next menstrual cycle (Day 8 of the menstrual cycle), to assay for concentrations of metabolites of estrogen and progesterone. This will objectively document the phase of the cycle as well as supply quantifiable information concerning hormone levels. Disproportionately low occurrence rates among female soldiers who do not go through a luteal phase for any reason will be evaluated as well.

**Progress:** This study has been terminated because the logistics of drawing and picking up samples at the TMC's, where most injuries are treated) have proven impossible with current personnel.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/035		<b>Status:</b> Completed	
<b>Title:</b> The Effects of Adrenomedullin and Angiotensin II on Fetoplacental Vascular Tone					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Nathan J. Hoeldtke, MC					
<b>Associate Investigators:</b> LTC Roderick T. Hume Jr., MC			MAJ Richard K. Wagner, MC LTC Byron C. Calhoun, MC		
<b>Key Words:</b> Placenta, vascular tone, adrenomedullin, angiotension II					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To investigate the effect of adrenomedullin on the human fetoplacental vascular tone. This will be investigated by evaluating changes in fetal circuit perfusion pressures in the isolated, dually perfused, human placental cotyledon. Effect on perfusion pressure will be evaluated by assessing changes in baseline pressure during the infusion of adrenomedullin and by assessing the vasculature's response to angiotensin II in the presence of adrenomedullin, compared with a control.

**Technical Approach:** We will use cotyledons from a total of 15 placentas obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery. A perfusate consisting of Hank's balanced salt solution, bovine albumin, heparin, and gentamicin, will be used to perfuse both the maternal and fetal circulations of the cotyledons. The perfusate will be maintained at a pH of 7.35 - 7.45 and gassed with 95% O2/5% N2. The cotyledons will be kept at 37 degrees Celsius.

The fetoplacental circuit of each study cotyledon will additionally be perfused with adrenomedullin in concentrations of 0.05 ng/ml, 5 ng/ml, or 50 ng/ml (five cotyledons with each concentration). Each fetoplacental circuit will then be successively challenged with the vasopressor, angiotensin II, with bolus doses of 0.005µg, 0.05µg, 0.5µg and 5µg. Fetoplacental vascular response will be assessed via changes in fetoplacental perfusion pressure. A control cotyledon from each placenta will also be injected with these doses of angiotensin II for comparison.

The baseline fetal perfusion pressure, before and after the addition of adrenomedullin in the fetal circuit, will be compared with a paired *t* test. Analysis of variance with repeated measures will be used to assess for differences in pressure changes between the control and study groups after angiotensin II dosing.

**Progress:** All data have been collected. Data analysis is in progress.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/080		<b>Status:</b> Completed	
<b>Title:</b> The Vasoactive Effects of Adrenomedullin on Fetoplacental Vasculature Precontracted with Endothelin-1 or the Thromboxane Mimetic, U46619					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Nathan J. Hoeldtke, MC					
<b>Associate Investigators:</b> LTC Roderick T. Hume Jr., MC			MAJ Richard K. Wagner, MC LTC Byron C. Calhoun, MC		
<b>Key Words:</b> vascular tone, adrenomedullin, cotyledon, endothelin-1, U46619					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To investigate the effect of adrenomedullin on human fetoplacental vascular tone. This will be investigated by evaluating changes in fetal circuit perfusion pressure in the isolated, dually perfused, human placental cotyledon. Changes in perfusion pressure will be assessed during the fetoplacental infusion of adrenomedullin after precontraction of the same vasculature with either endothelin-1 or the thromboxane mimetic, U46619.

**Technical Approach:** The fetoplacental circulation represents a low resistance vascular bed and factors controlling the vascular tone in this circulation remain to be fully elucidated. Adrenomedullin is a recently described hypotensive peptide which has been demonstrated to be present in amniotic membranes and fluid. Effects of this peptide, if any, on the fetoplacental vasculature have not been described. We will attempt to determine if this peptide is vasoactive in the fetoplacental circulation, distal to the umbilical flow, using dually perfused isolated human placental cotyledons. This test system is well established as a method of studying vasoactive substances in the fetoplacental circulation. We will use cotyledons from a total of 10 placentals obtained from uncomplicated vaginal and cesarean deliveries in MAMC's labor and delivery. A perfusate consisting of Hanks's balanced salt solution, bovine albumin, heparin, and gentamicin, will be used to perfuse both the maternal and fetal circulations of the cotyledons. The perfusate will be maintained at a pH of 7.35-7.45 and gassed with 95% O<sub>2</sub>/5% N<sub>2</sub>. The cotyledons will be kept at 37 degrees Celsius. The fetoplacental circuit of each study cotyledon will be precontracted with either U46619 or endothelin-1 (five cotyledons with each agonist). Each fetoplacental circuit will then be challenged with bolus doses of adrenomedullin (0.01 nmol-0.1 nmol), administered in a random sequence. Fetoplacental vascular responses will be assessed via changes in fetoplacental perfusion pressure. Fetal perfusion pressures, before and after the addition of each dose of adrenomedullin to the fetal circuit, will be compared with one way analysis of variance.

**Progress:** All data have been collected. Data analysis is in progress.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 92/101		<b>Status:</b> Completed	
<b>Title:</b> Neurodevelopmental Follow-Up of Infants of Mothers Who Seroconvert to HSV During Pregnancy					
<b>Start Date:</b> 09/04/92			<b>Est. Completion Date:</b> Mar 94		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Roderick T. Hume Jr., MC					
<b>Associate Investigators:</b> LTC Glenn C. Tripp, MC			Millie Herd, AN MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> herpes simplex virus, pregnancy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To evaluate infants of sero-converters by means of Denver Developmental Tests and type specific HSV antibodies by Western blot in order to answer the following questions: does maternal HSV-2 seroconversion during pregnancy without evidence of asymptomatic shedding of the virus from the genital tract at the onset of labor or evidence of acute neonatal HSV infection result in significant neurodevelopmental disability in the offspring; and can asymptomatic HSV seroconversion in the newborn occur as a result of in utero infection or undetected perinatal transmission without evidence of acute neonatal infection.

**Technical Approach:** About 3% of women who are HSV seronegative at the first prenatal visit are HSV seropositive at the time of delivery. If the maternal HSV cultures were negative on admission to the labor suite and the neonatal conjunctival and nasopharyngeal cultures were negative on day 2 of life, the newborns are discharged from the hospital at 1-5 days postpartum. The only long term follow-up performed has been routine pediatric care. However, any long term neurodevelopmental consequences to the uninfected offspring of women experiencing an asymptomatic first episode of genital HSV during pregnancy are unknown. This study will be done in conjunction with Children's Hospital, Seattle, WA, and the University of Washington. Approximately 20 children will be studied at Madigan. At six months of age, the child will be administered the modified Denver Developmental Test, and a blood sample will be drawn to measure type-specific HSV antibodies by Western blot. By six months of age, passively acquired maternal antibody should be completely metabolized. HSV antibody present at this time should represent an asymptomatic congenital or neonatal infection and seroconversion. Information regarding the mother's demographic profile and pregnancy history, her serologic and virologic profiles, and the infant data (e.g., birth weight, gestational age) will also be obtained.

**Progress:** This was a collaborative project between the University of Washington, Children's Hospital in Seattle, and Madigan Army Medical Center. Approximately 60 children were entered in FY 97 for a total of 1122 subjects. Results are summarized best by the conclusions of the NEJM article referenced below; "infection acquired near the time of labor is associated with neonatal herpes and perinatal morbidity." 4/9 neonates were infected; of these 1/4 died with sequela.

Publication: Brown, Z, Selke S, Zeh J, Kopelman J, Maslow A, et al: The Acquisition of Herpes Simplex Virus During Pregnancy. NEJM 1997; 337:509-515.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/144		<b>Status:</b> On-going	
<b>Title:</b> Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig (Sus scrofa)					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b>			COL Lawrence A. Decker, MC		
COL Gary D. Davis, MC			LTC Roderick T. Hume Jr., MC		
LTC Byron C. Calhoun, MC			Brown FE		
MAJ Richard K. Wagner, MC			MAJ Martin L. Ladwig, MC		
MAJ Christina Apodaca, MC					
<b>Key Words:</b> Gynecologic surgery, endoscopy, blowel, urinary tract, pig,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans. Familiarity with these techniques will allow an increased margin of safety for patients in gynecologic surgery and better prepare the gynecologic surgeon to assist in general surgery patients when bowel or urinary tract procedures or repair are required. Increased operative endoscopy experience will minimize operating time and potential complications when utilized in the clinical setting.

**Technical Approach:** With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

**Progress:** New protocol has not started.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/085		<b>Status:</b> Terminated	
<b>Title:</b> Operative Endoscopy and Surgical Management of the Bowel and Urinary Tract Injuries in Gynecologic Surgery in the Pig ( <i>Sus scrofa</i> ) and Goat ( <i>Capri hircus</i> )					
<b>Start Date:</b> 02/09/94			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b>			<b>COL Paul N. Smith, MC</b>		
LTC David J. Magelssen, MC			MAJ Rosemary L. Casey, MC		
MAJ Alicia Y. Armstrong, MC			MAJ Mary C. Nace, MC		
<b>Key Words:</b> Surgical management:gynecology, endoscopy, pig, goat,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b> 06/21/96	

**Study Objective:** 1) To familiarize residents in OB/GYN with techniques of management of bowel and urinary tract injury with suturing or stapling techniques. 2) To familiarize residents with techniques for colostomy, ileostomy, ureteroneocystostomy and vascular injury repair. 3) To expand the operative endoscopy experience of OB/GYN Residents and Staff, prior to utilization in humans.

**Technical Approach:** With the animal in the supine position, a midline incision will enter the abdomen and repair of lacerations and anastomosis will be performed by standard techniques. Additional surgical procedures may include ureteroneocystostomy. The abdomen will be closed. A second episode of surgery will occur 3-4 weeks later and additional procedures including colostomy, loop ileostomy, and vascular injury repair will be carried out. Following the second surgical episode, the animal will not be allowed to recover from anesthesia. In some cases an animal may be used for a single training episode. When this occurs, euthanasia will be carried out at the completion of the session. When follow-up evaluation of a surgical procedure is desired, no more than one procedure will be done on that animal during the first episode. The animal will then be allowed to recover and will be re-anesthetized and reoperated 3-4 weeks later. During the second surgical episode, more than one procedure may be performed. The animal will be euthanized at the end of the episode while still under general anesthesia. Procedures which would normally involve any postoperative care beyond normal husbandry will only be performed during the last surgical episode to which that particular animal is subjected. The animal will be euthanized while still under general anesthesia.

**Progress:** Three sessions utilizing 8 pigs were held on this protocol in FY 97. It was terminated in Jul 97 due to the expiration of the 3 year approval period. A new protocol is being written to replace it.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/051	<b>Status:</b> Terminated
<b>Title:</b> Caesarean Section Pain Study		
<b>Start Date:</b> 01/19/96	<b>Est. Completion Date:</b> Apr 96	
<b>Department:</b> Obstetrics/Gynecology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Jeffrey A. Rondeau, MC		
<b>Associate Investigators:</b>		
LTC Byron C. Calhoun, MC	LTC Joseph J. Mancuso Jr., MC	
CPT Frederick W. Larsen, MC	MAJ Nathan J. Hoeldtke, MC	
CPT Shelley B. James, AN	CPT Byron D. Gatlin, MC	
<b>Key Words:</b> Pain:cesarean, perioperative local anesthetic, IV narcotic therapy		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	9/30/97

**Study Objective:** To attempt to determine if perioperative local anesthetic injected into the incision line and the ilioinguinal nerves will improve post-operative pain control compared to standard intravenous narcotic therapy.

**Technical Approach:** This is a prospective, double-blinded study. After subjects are randomized to one of two study groups, spinal anesthesia using 1.6 cc of 0.75% bupivacaine with 0.2 mg epinephrine and 25 micrograms of fentanyl will be performed. After an adequate surgical block is obtained, 10 cc 0.5% bupivacaine with epinephrine 1:200,000 or saline control will be infiltrated along the proposed line of incision with an additional 5 cc placed to perform a bilateral ilioinguinal block (10cc total). A total of 20 cc of study solution or normal saline will be used prior to incision. Just prior to closure, the wound will be irrigated with 10cc of 0.5% bupivacaine with epinephrine 1:200,000 or saline control for a total of 30cc of study solution. The patient will receive perioperative prophylactic antibiotics using either Ancef 1gm IV or Cleocin 900mg IV as per protocol of the Department of Obstetrics. Post-operatively the patient will be placed on PCA (patient controlled anesthesia) using morphine with a concentration of 1mg/ml. The PCA will not be activated until the patient desires pain control. When reporting discomfort, the patient will receive a bolus of 5mg of morphine intravenously followed by activation of the PCA device. A continuous infusion will not be used so that actual narcotic requirement can be documented. The PCA dose and lockout interval will be 2mg and 8 minutes, respectively. If uncomfortable, the patient may receive a 5mg morphine bolus every four hours as needed. The patient will be given a flow sheet on which she will record verbal analogue pain scores at 1, 4, 8, 12 18, 24 hours postoperatively. The quantity of narcotic analgesic will also be tabulated for a 24 hour period at the same time interval as pain scores are assigned by the patient. Verbal analgesic usage on post operative days 1 and 3 will be recorded. Additional demographic data to include first time to ambulation, surgical complications, and surgical time, infant size, and blood loss will also be examined to determine influence on obtained data.

**Progress:** Approximately 35 patients were entered. The study was terminated because the randomization key was lost after the subjects were entered. Due to time restraints, the investigators decided not to repeat the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/138		<b>Status:</b> Terminated	
<b>Title:</b> Once vs Thrice Daily Gentamicin Dosing in Postpartum Endomyometritis					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Anne B. Shrout, MC					
<b>Associate Investigators:</b> CPT Scott M. Kambiss, MC			MAJ Jerome N. Kopelman, MC		
<b>Key Words:</b> endomyometritis, gentamicin, dosing					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To evaluate the once-daily dosing of gentamicin compared to the usual thrice-daily regimen of gentamicin in the treatment of postpartum endomyometritis and in patients with chorioamnionitis that undergo cesarean section.

**Technical Approach:** Patients will be enrolled from the patient population at Madigan. They must be diagnosed with postpartum endomyometritis or with chorioamnionitis and subsequent cesarean section. Patients will be randomized into two arms. Group 1 will receive the standard gentamycin 1.75 mg/kg every 8 hours IVPB with clindamycin 900 mg every eight hours. Group 2 will receive gentamycin 5.25 mg/kg every 24 hours IVPB and clincamycin 900 mg every eight hours IVPB. Both groups will have frequent drug levels obtained from a heplug in the opposite arm. All patients will remain on antibiotics until afebrile X 48 hours. Clinical response and failure will be determined by chi-square.

**Progress:** No further work was done on this study in FY 97. Thirteen subjects had been entered in previous years. Several similar studies were reported so the PI did not continue this protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/114		<b>Status:</b> On-going	
<b>Title:</b> The Effects of Lipopolysaccharide, an Inflammatory Stimulus, on Placental Production of Interleukin 6 in the Isolated Dually Perfused Placental Cotyledon					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard K. Wagner, MC					
<b>Associate Investigators:</b>			MAJ Christina Apodaca, MC		
MAJ Nathan J. Hoeldtke, MC			CPT Bruce F. Arnold, MC		
MAJ Roger M. Hinson, MC			LTC Byron C. Calhoun, MC		
LTC Roderick T. Hume Jr., MC					
<b>Key Words:</b> Interleukin 6, placental cotyledon, lipopolysaccharide					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		9/30/97	
\$0		\$0.00			

**Study Objective:** To determine the effects of inflammatory stimuli on placental production of Interleukin 6 (IL-6). This will be investigated in the isolated, dually perfused, human placental cotyledon in two steps: 1) by determining the constitutive production of IL-6 over time, and 2) by measuring production of IL-6 over time after stimulation by lipopolysaccharide (LPS). Levels of IL-6 in the fetal compartment of the placental cotyledon will be determined by sampling effluents from the fetal venous return and utilizing commercially available assays for IL-6. This is a pilot study to investigate the utility of the placenta model as a platform for further research on inflammatory cytokines in the perinatal period.

**Technical Approach:** We will use cotyledons from approximately 12 placentas (24 cotyledons) obtained from uncomplicated vaginal and caesarean deliveries in MAMC's labor and delivery. A perfusate consisting of Hank's balanced salt solution, bovine albumin, heparin, and gentamicin will be used to perfuse both the maternal and fetal circulations of the cotyledons. The perfusate will be maintained at a pH of 7.35-7.45 and gassed with 95%O<sub>2</sub>/5%N<sub>2</sub>. The cotyledons will be kept at 37 degrees Celsius. After establishing perfusion of an intact fetoplacental circuit, venous effluents will be collected at regular intervals and these samples will be stored for determination of IL-6 levels. The fetoplacental vascular tone will be continuously monitored throughout the experiment. Cellular changes resulting from the perfusion and inflammatory stimulus will be evaluated histologically by grading the inflammation present in biopsies taken before and after each experiment.

**Progress:** Study has not yet started, awaiting delivery of the needed supplies.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/044		<b>Status:</b> Completed	
<b>Title:</b> Plasma Levels of Adrenomedullin, A Hypotensive Peptide, in the Fetoplacental Circulation					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Obstetrics/Gynecology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard K. Wagner, MC					
<b>Associate Investigators:</b> Katherine H. Moore, Ph.D. LTC Roderick T. Hume Jr., MC			MAJ Nathan J. Hoeldtke, MC LTC Byron C. Calhoun, MC		
<b>Key Words:</b> Adrenomedullin, plasma, fetus					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine whether adrenomedullin is present in the plasma of the term human fetus. This will be investigated by evaluating arterial and venous umbilical cord blood obtained at delivery, with a radioimmunoassay specific for adrenomedullin. In addition, if adrenomedullin is identified in this circulation, a secondary objective will be to determine if the venous and arterial concentrations are different.

**Technical Approach:** We will use paired blood samples (venous and arterial cord blood) obtained from a total of 20 uncomplicated vaginal deliveries in MAMC's labor and delivery. Plasma will be obtained from these blood samples and stored at -70°Celsius until all the samples have been collected.

Peptides will be extracted from the plasma using C18 Sep-columns.

Radioimmunoassay will be performed, using a commercially prepared kit, with the following steps:

- 1) Rabbit antiserum will be added to standard and samples.
- 2) Tubes will be incubated overnight at 4°C.
- 3) 125I-Adrenomedullin will be added to each tube
- 4) Tubes will be incubated overnight at 4°C.
- 5) Goat Anti-Rabbit IgG serum and Normal Rabbit serum will be added to each tube.
- 6) Tubes will be incubated at room temperature for 90 minutes.
- 7) RIA buffer will be added to each tube.
- 8) Tubes will be centrifuged at 1700 g for 20 minutes.
- 9) Supernatant will be aspirated off.
- 10) Assay tubes will be evaluated with a scintillation well gamma counter.

If adrenomedullin is demonstrated in the cord blood, a comparison of the venous and arterial concentrations will be made with a paired *t* test. The significant level used will be  $p < 0.05$ .

**Progress:** Forty samples were analyzed. There was no difference between the adrenomedullin levels in the fetal umbilical vein and the fetal umbilical artery.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF PEDIATRICS**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/085		<b>Status:</b> On-going	
<b>Title:</b> Parental Assessment of Psychologic Adjustment in Children with Asthma: A Comparison of the Child Behavior Checklist and the Behavior Assessment System for Children					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jul 95		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Veronica R. Baechler, MC					
<b>Associate Investigators:</b> MAJ Robert A. Byrne, MS			COL Patrick C. Kelly, MC MAJ Stephen E. Greefkens, MC		
<b>Key Words:</b> Asthma;psychologic adjustment, Child Behavior Checklist, Behavior Assessment System for Children					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** 1) To assess the correlation between the Child Behavior Checklist (parent report) and the Behavior Assessment System for Children (parent report) in assessing the social and emotional status of a group of children and adolescents with asthma. 2) To assess the impact of disease severity on the social and emotional status of this population. 3) To assess the impact of moves or service member deployment on the social and emotional status of this population.

**Technical Approach:** Sixty subjects, ages from 8 to 16 years and including approximately equal number of males and females, who have chronic asthma will be identified through review of Pediatric Pulmonary Clinic files and review of upcoming appointments. After consent has been obtained the mother of these subjects will be asked to fill out both the CBCL and the Parent Report Form of the BASC. In addition, a brief questionnaire inquiring about the subjects health status, recent moves, and service member deployments will be completed by the mother. When data collection is complete, it will be analyzed as follows. Correlation between the various scales of the CBCL and BASC will be analyzed using paired t-tests. ANOVA will be used to study the relationship between disease severity and several scales on the CBCL. An unpaired t-test will be used to study the relationship between recent moves or parent deployment and several scales on the CBCL.

**Progress:** 13 subjects were entered in FY 97, for a total of 43 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/137		<b>Status:</b> Completed	
<b>Title:</b> The Relationship of Positive Skin Tests to House Dust Mite, Grass Pollen, and Cat Dander to Asthma in Children Presenting to a Pediatric Pulmonary Clinic					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Edward R. Carter, MC					
<b>Associate Investigators:</b> CPT Jeffrey W. Delaney, MC Troy H. Patience, B.S.			MAJ Evan J. Matheson, MC COL Donald R. Moffitt, MC		
<b>Key Words:</b> Asthmadust mite, grass pollen, can dander, minors					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine the following in children who attend the MAMC Pediatric Pulmonary Clinic: (1) the prevalence of positive skin tests to house dust mite (2 species), cat dander, and grass pollen in children with asthma  $\geq 4$  years old; (2) whether there is positive correlation between severity and chronicity of asthma and positive skin tests, especially to house dust mites; (3) whether there is positive correlation between the age of the child with asthma and the probability of having a positive skin test; (4) whether there is positive correlation between signs/symptoms of allergy and positive skin tests, especially to house dust mites in children with asthma; (5) relationships between total serum IgE, blood eosinophilia, asthma, and allergy in asthmatic patients and to establish the predictive value of these serologic tests for skin test positivity in asthmatics; and (6) to devise an algorithm for deciding which children need an allergy referral, which children should undergo environmental controls without a formal allergy assessment, and which children have such a low risk for allergy that no allergy assessment is necessary.

**Technical Approach:** A total of 100 to 200 children  $\geq 4$  years old with asthma presenting to the MAMC Pediatric Pulmonary Clinic for evaluation will be asked to participate in this observational study. Children who meet the diagnostic criteria for asthma will be eligible. Severity of asthma will be categorized as mild, moderate, or severe, based upon test criteria. Asthma will also be categorized as chronic or intermittent based upon the frequency of signs/symptoms. We will make all attempts to include consecutive children to ensure a representative sample. Subjects will complete a questionnaire and a complete history and physical will be performed. Blood will be drawn for serum IgE and peripheral blood eosinophil determination. They will receive skin prick tests for sensitivity to house dust mite, grass pollen, cat dander and 2 controls. We will determine the frequency of positive skin tests in this sample and assess the relationships between positive skin tests and patient age, severity and chronicity of asthma, signs/symptoms of allergy, an elevated serum total IgE, and blood eosinophilia. Data analysis methods will include chi-square for presence or absence of an effect on positive skin test for each variable. Multiple regressions will be performed for positive skin tests as a whole and then individually for each of the 3 specific skin tests. These regression analyses will determine which variables or combination of variables that best predicts a positive skin test in these asthmatic children.

**Progress:** Ninety-five subjects were enrolled in this study between August 1995 and September 1996; 1997 was spent analyzing the data. No serious complications were seen. The preliminary data shows that serum IgE was a good predictor of allergy as was serum IgE.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/126	<b>Status:</b> On-going
<b>Title:</b> Long-Term Use of Every 4-8 Week Intramuscularly Administered Triamcinolone Acetonide to Treat a 13 Year-Old Who Has Severe, Life-Threatening Chronic Asthma		
<b>Start Date:</b> 07/18/97	<b>Est. Completion Date:</b> Aug 98	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Edward R. Carter, MC		
<b>Associate Investigators:</b>		
CPT Victoria W. Cartwright, MC		MAJ Donald R. McClellan, MC
MAJ William R. Raymond IV, MC		MAJ Robert W. Moore, MC
<b>Key Words:</b> Asthma, triamcinolone acetonide, long-term		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To determine whether triamcinolone acetonide, a long acting corticosteroid preparation, if administered intra-muscularly on an every 4-8 week basis, can control asthma symptoms and airways obstruction without causing unacceptable adverse effects in a 13 year-old boy with severe life-threatening asthma who had complied poorly with prescribed medical regimens.

**Technical Approach:** After a baseline assessment the patient will receive 80 mg of triamcinolone acetonide intramuscularly. He will then continue to receive this dosage every 4-8 weeks. The dosing interval will depend upon clinical status (pulmonary function tests, signs/symptoms) and adverse effects (including the degree of adrenal suppression). The dosage and dosing interval will be altered based upon clinical response, pulmonary function tests, and the magnitude of adverse effects. The dosage and dosing interval will range from 40-80 mg and q 4-8 weeks respectively. The patient will continue to receive this steroid regimen for 12 months while being closely monitored.

**Progress:** The subject has been enrolled and been given two treatments. He is more active and is actually participating in some sports.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 90/092		<b>Status:</b> On-going	
<b>Title:</b> Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses					
<b>Start Date:</b> 07/20/90			<b>Est. Completion Date:</b> Sep 91		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mary P. Fairchok, MC					
<b>Associate Investigators:</b> MAJ Thomas A. Perkins, MC COL Marvin S. Krober, MC			COL James S. Rawlings, MC LTC Joanna C. Beachy, MC		
<b>Key Words:</b> HIV,diagnostic assays,children					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

**Technical Approach:** This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children. This analysis will be done in 120-150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

**Progress:** No subjects were entered during FY 97, a total of 3 subjects have been entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/060		<b>Status:</b> Completed	
<b>Title:</b> Single Dose Intramuscular Dexamethasone Acetate vs. Oral Prednisone to Treat Exacerbations of Asthma in Young Children					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Delores M. Gries, MC					
<b>Associate Investigators:</b> COL Donald R. Moffitt, MC			LTC Edward R. Carter, MC Janice Gibbons, M.D.		
<b>Key Words:</b> Asthma, dexamethasone acetate, prednisone, children					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study objective:** 1) To determine whether a single intramuscular dose of dexamethasone acetate is as effective as a five-day course of oral prednisone in resolving mild-moderate asthma exacerbations in young children. 2) To determine any differences in tolerance and/or adverse effects between a single dose of IM dexamethasone acetate and a 5-day course of oral prednisone in young children with mild-moderate exacerbations of asthma.

**Technical approach:** 20 children ages six months to seven years old who present to the MAMC Pediatric Clinic with acute exacerbations of asthma will be eligible to enroll in this prospective, randomized, investigator-blinded study. Patients will be randomized to receive either a single IM dose of dexamethasone or prednisone taken orally each day for five days. Dose will be adjusted for the age of the child. Data to be collected include, a complete physical examination at study entry along with wheeze and cough scores. On days 3 and 7 parent/guardian will be contacted by telephone and wheeze and cough scores, number of doses of albuterol used and tolerance of the treatment will be collected. On days 5 and 14, a complete physical exam will be repeated along with the measures collected on days 3 and 7. In addition an overnight timed urine collection for cortisol determination will be performed. On day 28 a final telephone call will be made to determine the number of patients who suffer a second asthma exacerbation within one month of the study. In addition the following data will be collected, number of treatment failures, time taken for patients to clear the asthma symptoms, number of patients who relapse within one month of the study, number of patients who require emergency department visits and hospitalization for asthma within one month of starting the study, patient satisfaction and complications.

**Progress:** Thirty-three patients were entered in FY 97, with one patient withdrawn due to retreatment. There were no adverse effects. Data analysis is in progress.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/004	<b>Status:</b> Completed
<b>Title:</b> Evaluation of Anti-inflammatory Actions of Perfluorophenanthane; Effects of Macrophage IL-6 Secretion on the BALB/c Mouse ( <i>Mus musculus</i> )		
<b>Start Date:</b> 10/18/96	<b>Est. Completion Date:</b>	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Roger M. Hinson, MC		
<b>Associate Investigators:</b> LTC Edward R. Carter, MC		
<b>CPT Victoria W. Cartwright, MC</b>		
<b>Key Words:</b> Macrophage, IL-6, perfluorophenanthane, mouse, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To evaluate the effects of perfluorophenanthane on macrophage secretion of IL-6 *in vivo* and *in vitro* using BALB/c mouse model

**Technical Approach:** This study is designed to test the hypothesis that *in vivo* exposure to perfluorocarbon downregulates inflammatory cytokine release by macrophages. This will be evidenced by a decrease in both the constitutive and stimulated secretion of IL-6 by macrophages *in vivo* and *in vitro*. The pristane mouse model offers a method to study the effects of the perfluorocarbon, perfluorophenanthane, on macrophage function *in vivo*. Groups of BALB/c mice will each receive intraperitoneal injections of either perfluorophenanthane or pristane; a control group will be treated in a similar fashion but will not receive any injections. Lavage samples of these mice will be obtained at day 60, coinciding with the onset of peak production of IL-6. The concentration of IL-6 will be determined in the lavage fluid. Macrophages obtained from lavage will be placed in cell culture. Macrophage production of IL-6 will be determined in unstimulated and LPS-stimulated cells for samples obtained from perfluorophenanthane and pristane primed mice. Should perfluorophenanthane attenuate IL-6 production in these experiments, another set of experiments will be performed to determine if concomitant administration of perfluorophenanthane and pristane will lead to a decreased inflammatory response to pristane *in vivo*. Macrophages will be cultured *in vitro* as above and IL-6 production determined. Statistical analysis of IL-6 levels will be performed using student's t-test and analysis of variance as indicated.

**Progress:** This protocol has been completed. The data indicate that, in the mouse model, perfluorophenanthane was not anti-inflammatory but rather was mildly pro-inflammatory, though much less so than pristane. These results contrast with several *in vitro* studies which have demonstrated decreased inflammatory mediator production by PFC laden macrophages. Possible explanations for this include differences in the methods of inducing inflammation, the model used to assess inflammation, and the brand of PFC used. Our study suggests that PFC may actually induce IL-6 production and potentiate the inflammatory response. These findings do not support the hypothesis that the decreased pulmonary inflammation noted in infants ventilated with PFC is due to direct anti-inflammatory effects of PFC. A presentation was made at the Conference on Military Perinatal Research.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/080		<b>Status:</b> Completed	
<b>Title:</b> MgSO4 Therapy for the Prevention of Intracranial Hemorrhage and Cerebral Palsy in the Very Low Birthweight Infant: Role of Interleukin-6					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Roger M. Hinson, MC					
<b>Associate Investigators:</b> MAJ Karen M. Nelson, MC			Robert Mittendorf, M.D., Ph.D.		
<b>Key Words:</b> Intracranial hemorrhage; cerebral palsy, interleukin-g, magnesium sulfate					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine whether an association exists between the inflammatory cytokine interleukin-6 and intracranial hemorrhage or cerebral palsy and if so, is this relationship altered by antenatal administration of magnesium sulfate.

**Technical Approach:** This study is designed to test the hypothesis that very low birth weight infants with intracranial hemorrhages and/or cerebral palsy will have elevated interleukin-6 cord blood levels as compared to normal controls and that antenatal administration of magnesium sulfate will alter the cord blood levels of interleukin-6. The cord blood samples will be provided through an ongoing protocol at the University of Chicago investigating whether MgSO<sub>4</sub> therapy can prevent intracranial hemorrhage or cerebral palsy in the very low birth weight infant. This protocol is concerned only with the blinded evaluation of the cord interleukin-6 levels. It is anticipated that approximately 200 patients will be enrolled resulting in the same number of samples to be tested. Interleukin-6 bioactivity will be determined by the B9 bioassay and antigenic interleukin-6 will be determined by commercial ELISA. The data will be presented graphically and associations between IL-6, Mg therapy and cord serum level, clinical and histopathologic evidence of chorioamnionitis and outcomes will be evaluated. Differences in IL-6 levels will be tested for statistical significance by t-test. Outcomes will be evaluated by an appropriate non-parametric test such as chi-square.

**Progress:** Approximately 180 patients were entered at the University of Chicago in this cooperative protocol. Samples were analyzed at MAMC. Data analysis and an abstract are being prepared by the University of Chicago.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/025	<b>Status:</b> Terminated
<b>Title:</b> Fetal Development: Are Undiagnosed Maternal Inborn Errors of Metabolism Associated With Poor Intrauterine Growth and Congenital Malformations in the Developing Fetus		
<b>Start Date:</b> 12/17/93	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Roger M. Hinson, MC		
<b>Associate Investigators:</b>		
James R. Wright, M.T.	Katherine H. Moore, Ph.D.	
LTC Arthur S. Maslow, MC	MAJ Jerome N. Kopelman, MC	
CPT Andrew J. Bauer, MC	MAJ Katherine S. Foley, MC	
MAJ Thomas D. Carver, MC	MAJ Nathan J. Hoeldtke, MC	
<b>Key Words:</b> metabolism, fetal development, malformations, fetal death		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To determine if previously undiagnosed maternal inborn errors of metabolism (amino acidemias or organic acidurias) are a significant cause of fetal growth retardation, fetal malformations and fetal demise.

**Technical Approach:** In this controlled prospective study, the serum amino acid and urine organic acid contents will be evaluated in 3 groups of pregnant women. Group 1 will consist of women who have had 2 or more spontaneous abortions, a stillbirth, or have delivered a child identified as growth retarded, microcephalic, mentally retarded or with congenital anomalies. Group 2 will be the control group and consist of women who have had no more than 1 spontaneous abortion, or have delivered children with no known anomalies or are pregnant for the first time. Group 3 will consist of women not previously enrolled who are found during the pregnancy to have a fetus which is growth retarded ( $\leq$  3rd percentile on two ultrasounds 3-4 weeks apart), is microcephalic ( $\leq$  3 percentile on 2 ultrasounds 3-4 weeks apart), or has congenital anomalies.

The study questionnaire will be filled out at the time of entrance into the study and will consist of information pertaining to maternal educational and health history.

All samples will be sent to clinical investigation for storage until they can be analyzed. The blood samples will be frozen at -70 C until analyzed for quantitative amino acid content. The urine sample will be analyzed by GD Mass Spectroscopy for organic acid content. If both are normal then no further investigation will be done. If both are abnormal compared to published standards, the appropriate diagnostic work-up will be done to further identify the abnormality. All samples will be collected after an 8-12 hour fast to avoid post-prandial fluctuations in amino-acid concentrations. The study participants will be notified of their individual results (if abnormal) as they become known.

**Progress:** Data were lost due to a computer malfunction. The project was then terminated due to the departure of the principal investigator.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/056		<b>Status:</b> On-going
<b>Title:</b> Physiological, Behavioral, and Feeding Effects of Neonatal Physical Therapy Procedures on Preterm Infants in a Neonatal Intensive Care Unit Setting				
<b>Start Date:</b> 02/21/97		<b>Est. Completion Date:</b> Oct 99		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Jane K. Sweeney, Ph.D., PT, PCS				
<b>Associate Investigators:</b> W. Barfield		MAJ Roger M. Hinson, MC		
<b>Key Words:</b> Physical therapy, preterm infants, NICU				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** a) To study and compare the physiological tolerance of medically stable, preterm infants to three interventions: neonatal hydrotherapy, infant seat positioning with social stimulation, and a control intervention of no physical handling or social stimulation; b) to investigate and compare the behavioral tolerance of medically stable, preterm infants to three interventions in a neonatal intensive care unit: neonatal hydrotherapy, infant seat positioning with social stimulation, and a control intervention of no physical handling or social stimulation; c) to evaluate and compare the effects of neonatal hydrotherapy, infant seat positioning with social stimulation and a control condition of no handling or social stimulation on oral feeding performance in medically stable, preterm infants; d) to compare the length of hospital stay among subjects in the three intervention groups.

**Technical Approach:** This is a prospective, quasi-experimental study of the physiological, behavioral, feeding, and cost effects of neonatal physical therapy procedures on 60 medically stable, preterm infants (31 to 35 weeks post-conception) in a neonatal intensive care unit setting. A randomized block design is used with postconceptual age as the blocking variable. After an 10 minute initial baseline phase, subjects are randomly assigned to a physical therapy intervention followed by oral feeding and concluded by a 10 minute recovery baseline phase. The intervention conditions are a 15 minute session of neonatal hydrotherapy (20 subjects), infant seat positioning with social stimulation (20 subjects), or a control condition of no handling (20 subjects). The physiological measures of heart rate, respiratory rate, mean arterial pressure, temperature, intracranial pressure, and oxygen saturation are recorded continuously and will be compared across intervention groups among the four phases of the study using a repeated measures analysis of variance. The behavioral responses of behavioral state, motor stress cues (finger splay, arm salute, trunk arch), and autonomic stress cues (hiccoughs, sneezes, yawns, regurgitation) are measured continuously by videotape and scored at two minute intervals. Between group comparisons of behavioral responses will be analyzed by analysis of variance (ANOVA). Feeding performance of volume ingested, duration of feeding, transition from gavage to oral feedings and weight gain will be reported descriptively and compared across intervention groups with ANOVA. The length of hospital stay and estimated cost of hospitalization in the NICU will be calculated and compared among all intervention groups using ANOVA.

**Progress:** 2 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/008		<b>Status:</b> Completed	
<b>Title:</b> Effect of Short Course High Dose Corticosteroids on the Immune Response to the Influenza Vaccine in a Pediatric Population					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Pediatrics			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Daniel P. Trementozzi, MC					
<b>Associate Investigators:</b> LTC Edward R. Carter, MC			MAJ Mary P. Fairchok, MC		
<b>Key Words:</b> Influenza, immune response, pediatric, corticosteroids					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** 1) To study the effect of short course high dose oral corticosteroids on the immune response to the influenza vaccine in young asthmatics. 2) To increase awareness of the need for annual influenza immunization in a high risk pediatric population.

**Technical Approach:** One hundred sixty pediatric patients recommended to receive the influenza vaccine will be enrolled. Of these, half will be subjects with asthma who present to the pediatric clinic with a flare of their asthma and who require treatment for a short, 5-day course of high dose oral prednisone. The remaining half will be either healthy siblings of asthmatics or asthmatics who are both asymptomatic at time of enrollment and who have not received oral steroids within three weeks prior to beginning the study. All subjects will receive one dose of the 1995-96 inactivated, split influenza vaccine at a dose of 0.5 cc, given IM. Blood will be drawn just before and 2-3 weeks after vaccination and influenza titers will be determined. Patients will be categorized as responders if they demonstrate a fourfold rise in serum titers to influenza following vaccination.

**Progress:** Fifty-eight patients were entered in the study; eight dropped out; 19 were in the treated group, and 31 in the control group. There were no significant differences in the groups.

DETAIL SHEETS FOR PROTOCOLS

PHYSICAL MEDICINE AND  
REHABILITATION SERVICE

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/098		<b>Status:</b> Completed	
<b>Title:</b> A Randomized Clinical Trial of A Home Program Monitored by a Physical Therapist versus Repeated Outpatient Physical Therapy Visits Combined with Home Program to Treat Stiff Shoulder					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Physical Medicine & Rehabilitation Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Lynn C Burke					
<b>Associate Investigators:</b>			Kathleen Hummel-Berry		
<b>Key Words:</b> Stiff shoulder, home physical therapy, OP physical therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To compare physical therapy treatment of stiff shoulder using guided home program only, to a protocol of outpatient clinic based physical therapy which includes an identical guided home program of exercises, plus the use of physical agents and passive procedures.

**Technical Approach:** This will be a prospective randomized clinical trial comparing two forms of physical therapy for stiff shoulder; an individualized home program, and a protocol of physical therapy which combines home program with typical outpatient clinic interventions. One hundred sixty subjects (80 from Madigan Army Medical Center) will be recruited for this multi-center study. Eligible subjects referred to physical therapy will be asked to participate in the study. Therapists providing outpatient care must apply one physical agent (such as ultrasound or heat packs) and one passive technique (such as mobilization or stretching) at each clinic visit, choosing the specific agent and manual technique based on evaluation of the patient's individual needs. The home program of exercises will be the same for both groups, and will address posture correction, range of motion exercises, and education on safe levels of functional activity. Thus, the only difference in the treatment provided to the two groups will be the fact that additional procedures take place in the outpatient therapy visits. Patients will receive treatment for a period of six weeks, or until treatment goals are attained (as judged by the physical therapist), whichever occurs first. Baseline pain level recorded as a value of 1-10, SF-36 and Simple Shoulder Test will be collected at the first physical therapy visit. The same three evaluative tools will be administered as follow-up measures every four weeks thereafter. The measures will be collected at physical therapy visits if patients are still attending physical therapy. They will be handed to the patients by physical therapists, but filled out independently by the patient. When the patient is no longer attending therapy, the measures will be collected by mail. If some patients fail to respond to this mailing, we will collect the SF-36, SST and pain level by telephone.

**Progress:** Eighteen patients were entered at MAMC in this multicenter study. Madigan in-pat is complete. Data analysis is to be done elsewhere.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/152	<b>Status:</b> On-going
<b>Title:</b> Cervical and Lumbar Radiculopathies: How Many Muscles Should Be Studied?		
<b>Start Date:</b> 09/20/96	<b>Est. Completion Date:</b> Jul 97	
<b>Department:</b> Physical Medicine & Rehabilitation Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Shashi J. Kumar, MC		
<b>Associate Investigators:</b>		
Liliana E. Pezzin, M.D.	Timothy D. Dillingham, M.D.	
LTC Steve S. Shannon, MC	MAJ Tamara D. Lauder, MC	
Andrew Gitter, M.D.	Michael Andary, M.D.	
	Andrew Haig, M.D.	
<b>Key Words:</b> Radiculopathy:cervical, Radiculopathy:lumbar		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** The primary objective of this study is to determine how many muscles must be studied in order to ensure a high rate of identification of those radiculopathies which can be electrodiagnostically confirmed. This observational, prospective study of consecutive patients will primarily involve data collection and analysis of standard electrodiagnostic studies. The electromyographic screen will be standardized for the upper limb and the lower limb. Two or three additional muscles will be studied beyond what is normally performed in the course of a clinical study.

**Technical Approach:** A multi-center study will be undertaken to provide approximately 700 subjects. Subjects will include all males and females on whom a cervical radiculopathy (CR) or LSR electrodiagnostic screen is performed. Data will be collected regarding the history, physical examination, and examiner assessment. All patients will have at least one motor and one sensory nerve conduction study. A standardized needle electromyography study will then be done for each extremity studied. A 10 muscle screen will be performed on the upper extremity to look for a CR and an 11 muscle screen will be performed on the lower extremity studied to look for a LSR. Any other additional nerves or muscles may be studied at the discretion of the electrodiagnostician if they are needed to make a clear diagnosis. Data analysis will be carried out similar to previous retrospective studies. In order to determine how many muscles are needed to identify the CR or LSR, various muscle screens will be combined and their identification rates will be analyzed using an SPSS database. The sensitivity of the radiculopathy screens will be evaluated relative to gold standards such as MRI, CT, or myelography on those subjects whom have such studies available. Specificity will not be evaluated as we are not recruiting normal subjects. Analysis of variance will be used to compare which head of the quadriceps and gastrocnemius is more sensitive in identifying a LSR. The relationship between the probability of paraspinal muscle abnormality and the above variables will be determined using a multi-variate probability (PROBIT) analysis. All data analysis will be done at John Hopkins University.

**Progress:** 50 subjects have been entered in FY 97, for a total of 150 subjects. Patient enrollment is still in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/023	<b>Status:</b> Terminated
<b>Title:</b> Deep Water Running as A Form of Rehabilitation for Ankle Inversuib Sprains: A Look at Maintenance of Land Based Running Performance and Long Term Training Effects		
<b>Start Date:</b> 12/15/95	<b>Est. Completion Date:</b> Oct 95	
<b>Department:</b> Physical Medicine & Rehabilitation Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Tamara D. Lauder, MC		
<b>Associate Investigators:</b> COL Shashi J. Kumar, MC		
<b>Key Words:</b> Running:deep water		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To provide a total non-weightbearing form of exercise which is more specific for land running and can be performed by a population with injuries that preclude them from weightbearing and/or land running. Specifically, service members with acute ankle sprains will be studied to (1) compare the percentage of subjects in each group which pass the APFT 2-mile run after rehabilitation, (2) compare each individual's post-rehabilitation 2-mile run time to their last pre-injury APFT 2-mile run time within the last year, (3) compare the results of a functional ankle test, consisting of both objective and subjective measures between the experimental group and the control group, and (4) to compare the rate of reinjury and reprofile for injury to the same ankle (requiring medical attention and medical record documentation) at 6 months via a questionnaire.

**Technical Approach:** The proposed study will look at rehabilitation methods for acute ankle sprains. Approximately 120 active duty male subjects with acute ankle sprains will be evaluated within 72 hours and randomized into a 4 week rehabilitation program of either (1) deepwater running with proprioceptive exercises or (2) the currently used acute ankle rehabilitation program through the Physical Therapy Department. Several outcome measures will be studied as described in the objectives. This data will be used to look for a significant difference among the individuals using the different rehabilitation methods.

**Progress:** Prior to FY 97, 15 patients were entered. Subject to work to be done on a grant research project and poor subject compliance, this project was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/006		<b>Status:</b> Completed	
<b>Title:</b> The Female Athlete Triad: Prevalence in Military Women					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Physical Medicine & Rehabilitation Svc			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Tamara D. Lauder, MC					
<b>Associate Investigators:</b> COL Gary D. Davis, MC			MAJ Marc V. Williams, MC LTC Richard A. Sherman, MS		
<b>Key Words:</b> Female athlete triad, military women, eating disorder, amenorrhea, osteoporosis					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					11/15/96

**Study Objective:** To determine the prevalence of the female athlete triad in the female military population at Ft. Lewis, WA. The female athlete triad is the coincidence of 1) pathologic eating behaviors, 2) exercise-induced amenorrhea, and 3) low bone mineral density.

**Technical Approach:** The Eating Disorder Inventory (EDI, part 1), a questionnaire, will be sent to all active duty females at Ft. Lewis (approximately 3430). Those subjects fitting the criteria for pathogenic eating behavior will be asked to complete the EDI, part 2 and the Scheduled Diagnostic DSMIV for Eating Disorders (SCID) and to come for a clinical interview. Subjects with pathogenic eating behavior and a history of amenorrhea will undergo clinical evaluation and laboratory workup by the gynecology department to determine the cause of amenorrhea. The subset of these women with amenorrhea attributable to exercise will undergo bone densitometry of the vertebral column.

**Progress:** 423 active duty women and 310 ROTC cadets completed the study. An abstract has been presented to the American College of Sports Medicine.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/157	<b>Status:</b> Completed
<b>Title:</b> The Effect of Pregnancy on the Performance, Health, and Nutritional Status of Postpartum Soldiers		
<b>Start Date:</b> 09/21/94	<b>Est. Completion Date:</b> Sep 95	
<b>Department:</b> Physical Medicine & Rehabilitation Svc	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> COL Joseph R. Dettori, SP		
<b>Associate Investigators:</b> LTC Kathleen A. Westphal, MC CPT Anthony Pusateri, MS	COL Paul N. Smith, MC LTC Alana D. Cline, MS CPT Teresa M. Vanderlinde, MC	
<b>Key Words:</b> female soldiers:pregnancy, health		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** (1) To determine the proportion of soldiers who return to their preconception fitness level at their first postpartum APFT, and to compare; (2) distribution, incidence and risk of injury and illness between postpartum soldiers and nonpregnant, non-postpartum soldiers; (3) changes in weight and body composition between soldiers and family members in the postpartum period; (4) bone mineral status between late pregnant and postpartum soldiers and their family members; (5) nutritional status between late pregnant and postpartum soldiers and family members; (6) iron and folate status among late pregnant and postpartum soldiers, late pregnant and postpartum family members, and nonpregnant, non-postpartum soldiers.

**Technical Approach:** Women in their third trimester of pregnancy will be identified through the OB-GYN clinics at their respective hospitals and asked to volunteer for the study. Non-pregnant soldiers will be solicited through the unit chain of command.

Full-time health personnel hired for the study at each site will measure the dependent variables and collect the data. Study health personnel will be supervised by an Army obstetrician. Study subjects will undergo blood draws to assess iron, folate and calcium status; anthropometric measurements to determine body composition, dual energy x-ray absorptiometry to measure bone mineral density and to validate body fat evaluations. Fitness will be assessed using the last pre-pregnancy Army Physical Fitness Test scores and the first postpartum APFT scores for all soldiers in the study. Medical records of all soldiers will be reviewed monthly to record all injuries and illnesses. Demographics, health habits and diet history, and exercise before, during and following pregnancy will be obtained through questionnaires.

**Progress:** 468 subjects were studied. 48% of the soldiers failed to return to pre-pregnancy fitness level 6-9 months postpartum. These postpartum soldiers were four times more likely to fail the APFT at the first postpartum fitness test as compared to non-pregnant female soldiers. These data support the popular trend in the Army to initiate a mandatory, graded postpartum PT program specifically targeted to this population. There is a rise in injury and illness rates for postpartum soldiers. Poor nutrition associated with trying to lose weight may contribute to this rate increase. There was also among postpartum women an increase in women who did not meet the Army weight standard as compared to non-pregnant women. Bone mineral density in trabecular bone was reduced in postpartum mothers and was increased in lactating mothers. Calcium levels and iron levels were all reduced in postpartum soldiers after delivery and had not returned to normal at 6-9 months.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Status:</b> Completed 97/	
<b>Title:</b> The Effects of Transcutaneous Electrical Nerve Stimulation on Delayed Onset Muscle Soreness			
<b>Start Date:</b> 12/19/96		<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> Physical Medicine & Rehabilitation Svc		<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Daniel C. Norvell, SP			
<b>Associate Investigators:</b> COL Joseph R. Dettori, SP		R.M. Wilson	
<b>Key Words:</b> Muscle:soreness, electrical nerve stimulation			
<b>Accumulative MEDCASE Cost:</b>	\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
		<b>Periodic Review:</b> 9/30/97	

**Study Objective:** The objective of this study is to determine whether or not transcutaneous electrical nerve stimulation (TENS) is effective in treating the signs and symptoms related to delayed onset muscle soreness (DOMS) in a male military population. Specifically, perceived pain, strength, and range of motion (ROM) will be assessed.

**Technical Approach:** The objective of this study is to determine whether TENS is effective in treating the signs and symptoms related to DOMS in a well-trained male population. We will include 60 active duty Army males who are not involved in competitive weight training and who have never experienced TENS. Subjects will be randomly assigned to receive a TENS treatment or a sham TENS treatment and assessed for pain, ROM, and strength. We will induce DOMS with repeated eccentric contractions of the elbow flexors. Subjects will return 48 hours post-exercise and be assessed for all measures. The treatment and placebo groups will receive the assigned treatment for 20 minutes. All subjects will be reassessed for pain, ROM, and strength immediately following the treatment. A final evaluation will be obtained 72 hours post-exercise. The data for the three measurements will be analyzed using repeated measures of ANOVA for each outcome measure.

**Progress:** Fifty-nine subjects were studied. The results indicate that transcutaneous electrical nerve stimulation may slightly decrease pain in soldiers with delayed onset muscle soreness, but it appears to be ineffective in improving the functional measures of active range of motion and eccentric strength.

**DETAIL SHEETS FOR PROTOCOLS**

**PREVENTIVE MEDICINE SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/011		<b>Status:</b> On-going	
<b>Title:</b> Comparative Morbidity Study of Active Duty Women Serving in Korea and Ft Lewis by MAJ Jeffrey D. Gunzenhauser, MC					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Jeffrey D. Gunzenhauser, MC					
<b>Associate Investigators:</b>			CPT Julie A. Pavlin, MC		
<b>Key Words:</b> Female soldiers, morbidity, Korea, Ft Lewis					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97	

**Study Objective:** To describe the out-patient and in-patient morbidity experience of women serving in Korea and compare this to women serving at Ft. Lewis and to men at both locations and to describe behavioral risk factors of women serving in Korea.

**Technical Approach:** This is an epidemiologic study. Out-patient clinical events which are assessed at military clinics will be categorized into one of 14 specific morbidity categories: orthopedic/injury, respiratory, medical illness, dermatologic, bites/stings, environmental injury, diarrhea/GI, unexplained fever, sexually transmitted disease, ophthalmic, mental health, dental, substance abuse and miscellaneous. Diagnosis will be based on medical record entries (not chief complaints) and will be broken down by gender. Rates of health care usage for men will be estimated by counting all visits registered in clinic logs. One male record will be pulled for each female record pulled (the second male to visit the clinic after the index female visit).

In-patient morbidity experience of women will be studied by analyzing data from the Individual Patient Data System maintained at Ft. Sam Houston, TX. All hospitalization of men and women will be included in the analysis. Each hospitalization at the 121 General Hospital and at Madigan AMC will be classified into one of the 14 morbidity categories to allow broader comparisons with out-patient morbidity data and between genders and locations.

Health surveys will be mailed to a probability sample of female soldiers serving in Korea and at Ft. Lewis. Approximately 1000 women in Korea and 1000 women at Ft. Lewis will be targeted for this survey.

**Progress:** No subjects were entered during FY 97. Collected data in previous FY (25,000 clinic visits) far exceeded expected number. Contractors were unable to complete data entry within budget. Balance of data entry was recently completed by MAMC personnel.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/019		<b>Status:</b> Completed
<b>Title:</b> The Risk of Myocardial Infarction Associated with Physical Inactivity in Young Women				
<b>Start Date:</b> 12/19/96		<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ David W. Niebuhr, MC				
<b>Associate Investigators:</b> Siscovik DS		LTC Margot R. Krauss, MC Schwartz S		
<b>Key Words:</b> Myocardial infarction, physical inactivity, young women				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** 1) To determine the relative risk of myocardial infarction (MI) associated with physical inactivity in young women. 2) To see if the relationship between MI and physical inactivity is strongest with energy expenditure, exercise duration, or intensity. 3) To adjust the relative risk of MI associated with physical inactivity for major cardiovascular disease risk factors such as smoking, hypertension, hypercholesterolemia, age, and oral contraceptive use.

**Technical Approach:** This study will attempt to determine the relative risk of MI in young women associated with physical inactivity. Secondary data analysis of the Low Dose Oral Contraceptives and Cardiovascular Disease study will be performed. The study design is a population based case control study of women residing in King, Pierce and Snohomish Counties, aged 18 to 44 years from January 1991 to December 1993. Data was collected by in-person interviews of cases, controls, and surrogates of fatalities, within three months of the incident event. Leisure time physical activity questions were derived from the Minnesota Leisure-Time Questionnaire. An unconditional logistic regression model will be developed. The outcome will be fatal and non-fatal MI. The predictors of interest will be intensity, duration, and energy expenditure of physical activity. Potential confounders to be examined are: age, race, education, smoking, hypertension, hypercholesterolemia, oral contraceptive use, and hormone replacement therapy.

**Progress:** 135 women with fatal and nonfatal myocardial infarction and 526 controls selected by random digit telephone dialing were mated by age. Physical inactivity was 4.4 times more common among women with MI. Final data analysis is in progress.

A poster presentation was made at the Prevention 97, Mar 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/159		<b>Status:</b> Completed	
<b>Title:</b> Relationship of Spouse and Child Abuse in A Military Population					
<b>Start Date:</b> 09/20/96			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Preventive Medicine			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Peter D. Rumm, MC					
<b>Associate Investigators:</b>			LTC Margot R. Krauss, MC		
Frederick Rivara, M.D., MPH			Michelle Bell, Ph.D.		
LTC Nancy K. Raiha, MS			Peter Cummings, M.D., MPH		
<b>Key Words:</b> Abuse:child, Abuse:spouse, military population					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** For many years there has been a perception that child and spouse abuse has a strong correlation in families. The Military Family Advocacy Program has tracked in a singular data set such abuse in families for seven years in almost 90,000 reported incidents. This study as outlined in the related thesis proposal and Department of the Army Family Advocacy Research Plans is the first documented attempt at looking at the correlation of spouse and child abuse in a large data set.

**Technical Approach:** The working hypothesis of this study (supported by preliminary data review) is that there is a higher rate of child abuse in families with pre-existing spouse abuse and that particular family characteristics may make some families at increased risk. The data set has been provided through the Family Advocacy Program (FAP) and contains 53 "fields" of information on each case of reported abuse from DA-2436. Additional information will be obtained from the FAP for DEERS data on the number of married couples with children in the Army for use in calculation or relative rates of abuse. The primary goal of the study will be to calculate the incidence of child abuse in families with already documented spouse abuse and compare that rate to the overall Army population of such families. In addition, stratified and logistical analysis of possible subgroups of families, i.e. by ranks, age of abuser, geographical location will be performed to identify groups of families at higher risk for "dual" abuse. There is a strong interest in the Army Family Advocacy Program to have such knowledge to predict families at increased risk.

**Progress:** A retrospective study compared families with children having documented spouse abuse (n=21,663) with Army families with children (n=271,191) to determine the relative risk of incident child abuse. Parameters which raised the relative risk factor for dual abuse were: low enlisted rank, 3 or more children, military father's age under 23, and several racial groups. The study demonstrated that spouse abuse is a strong risk factor for subsequent child abuse.

:

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF PSYCHOLOGY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/001		<b>Status:</b> Completed	
<b>Title:</b> Neurocognitive Functioning in Children with Chronic Idiopathic Thrombocytopenic Purpura					
<b>Start Date:</b> 10/18/96			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Mary G. Lambie, Ph.D.					
<b>Associate Investigators:</b> MAJ Robert A. Byrne, MS COL William O. Walker, Jr., MC			MAJ Robert I. Miller, MC, USAF Kenneth A. Zych		
<b>Key Words:</b> Purpura:thrombocytopenic, neurocognitive functioning, children					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: To determine if children with chronic Idiopathic Thrombocytopenic Purpura (ITP) are at increased risk of neurocognitive deficits as measured by standardized neuropsychological testing.

Technical Approach: This study will assess the neurocognitive functioning of children with Chronic Idiopathic Thrombocytopenic Purpura (ITP). Approximately 6-8 children (age 6-18) with (ITP) being followed in the Pediatric Hematology/Oncology Clinic at Madigan Army Medical Center will be assessed. In addition, 6-8 children diagnosed with Juvenile Rheumatoid Arthritis (JRA), matched for age will be assessed as a control group. All children in the study will have a physical and their medical records will be reviewed by a Pediatric Developmental Fellow to make sure they meet inclusion/exclusion criteria. Neuropsychological assessment will be conducted by a Pediatric Psychology Fellow. Measures used with the children will be (1) Wechsler Intelligence Scale for Children-III (WISC-III), (2) Purdue Peg Board, (3) Beery Developmental Test of Visual-Motor Integration (BDTVMI), (4) Trail Making Test (A&B), (5) Animal Naming, (6) Sensory Perceptual Exam, (7) Wide Range Assessment of Memory and Learning (WRAML)--Word List subtest. In addition, parents will complete the Behavioral Assessment Scale for Children (BASC). Data regarding the age at onset, duration of illness, last platelet count, bleeding phenomena, and therapy will be collected by parent report and a review of the medical record. The scores of each individual test will be converted to T-scores for comparison. A series of t-tests comparing the study group (children with chronic ITP) and the control group (children with JRA) for each individual test will be conducted. The scores for each subject in the study group will also be compared to national norms. It is hypothesized that children with ITP will exhibit neuropsychological deficits as compared to a chronic illness control group and national norms in the areas of behavior, attention/concentration, cognitive flexibility, visual-motor integration, visual-motor speed and coordination, and verbal fluency as measured by the above assessment tools.

Progress: Eleven subjects were entered. Data collection is complete and data analysis is in progress. The principal investigator has resigned from the Army.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/130		<b>Status:</b> On-going	
<b>Title:</b> MMPI-2 Profiles in Korean Military Dependents					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Kathleen S. Lester, MS					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Military dependents:Korean-born, MMPI-2					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		9/30/97
			\$0.00		

Study Objective: To determine the normative scores for the Minnesota Multi-phasic Personality Inventory-2 (MMPI-2) in Korean dependent wives of active duty soldiers.

Technical Approach: In order to determine the norms for the Korean female spouses of service members, the MMPI-2 will be administered to 50 subjects, age 20 to 70. Subjects will be recruited from the primary care clinics at MAMC by means of referral by their physician and through recruitment advertisements posted in community areas of Ft. Lewis. Subjects consenting to participate will be given a questionnaire, a brief, structured psychiatric interview (mini-SCID), a screening test of English proficiency and the MMPI-2. The mean and standard deviation of the clinical and validity scales will be derived for the group. These scores will be compared with existing norms and, where differences exist, t-tests of significance will be performed. Results will be examined for co-variance of factors of age, number of years in the U.S, and proficiency in English language.

Progress: 8 subjects were entered during FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/103		<b>Status:</b> Completed	
<b>Title:</b> Reports, Estimates, and Tests Results of Memory Functioning in Children With and Without ADHD: Concordance Between Self-Report, Parent-Report, Teacher-Report, and Test Results					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> James R. Masson, MD					
<b>Associate Investigators:</b> MAJ Robert A. Byrne, MS			Kenneth A. Zych		
<b>Key Words:</b> ADHD, memory, self-report					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To complete a pilot study in two steps in order to ensure that at least Step One, which could be a stand-alone pilot study, gets accomplished. (1) Complete a pilot study (N of at least 15) which yields an initial empirical sense of the concordance between and of the nature and relative reliability of child self-reports, parent-reports, teacher-reports, and test results of memory functioning in children diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD). (2) Once the minimal N of 15 children with ADHD is evaluated and tested to ensure a minimal pilot study, an additional minimal N of 15 children, with only minor medical ailments and no diagnosis of ADHS but some parental concern about memory functioning, will also be evaluated and tested. (3) (optional) Once Step One and Step Two have been ensured with minimal Ns of 15 children each it would be desirable to evaluate and test an additional minimal N of 15 children with only minor medical ailments and no diagnosis of ADHD and no parental concern about memory functioning.

**Technical Approach:** This study will proceed in two steps. The first step will collect data on memory functioning in a sample of 15 children diagnosed with ADHD, between 6 and 12 years of age, and the second step will repeat the same process in a group of children not diagnosed with ADHD, also between 6 and 12 years of age. Children with estimated IQs below 80 or who are physically unable to complete paper and pencil tests will not be included in the study. The information on memory functioning in each child will be obtained from the self-report of the child, direct memory testing of the child, and from reports by parents and teachers of the child. Measures used with child subjects will be (1) the EDMQ-C, (2) the BASC-SRP-C (for children aged 8-11 years) or the BASC-SRP-A (children of age 12) or BASC-PRS-C, and BASC-TRS-C ratings (for children 6 and 7 years of age), (3) the CVLT-C, (4) the Picture Memory and Design Memory nonverbal memory subtests of the WRAML, and (5) the TONI-2. Measures used with parents will be the EDMQ-P, the BASC-PRS-C (for children aged 6-11 years) or BASC-PRS-A (for children of age 12), and the PNIR-P. Measures used with teachers will be the EDMQ-T, the BASC-TRS-C (for children aged 6-11 years) or BASC-TRS-A (for children of age 12), the APRS, and the PNIR-T. The data analysis will be correlational, using Gorsuch's UniMult, and focused on the concordance between child, parent, and teacher reports of memory functioning in children. Post hoc comparisons will use "protected F or t-tests."

**Progress:** Twenty-four subjects were entered. Data analysis is in progress. The principal investigator has completed his training and left MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/108		<b>Status:</b> Terminated	
<b>Title:</b> Medical Cost Offset and Clinical Effectiveness of a Behavioral Treatment Program for Medical Resource Overutilizers					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Jan 96		
<b>Department:</b> Psychology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John B. Powell, MS					
<b>Associate Investigators:</b> Carol Ellsworth, MBA			Mary Brencick, MSW Anita Millman-Thorndyke		
<b>Key Words:</b> medical resources, overuse, treatment program					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

Study Objective: This study will identify patients with few physical findings and whose presenting complaints are produced or aggravated by psychological, rather than organic, factors, and to provide a brief, effective behavioral intervention designed to ameliorate these psychological factors.

Technical Approach: This study will follow 100 patients referred from the Adult Primary Care Center, and compare them to 100 non-treatment controls. Patients will complete a four week behavioral program consisting of four weekly classes and four individual biofeedback sessions. medical usage for the six months prior to treatment (including outpatient visits, inpatient treatment, laboratory procedures, and pharmacy costs) will be compared to usage for the six months post treatment.

Progress: No subjects have been entered in FY 97. Study is being terminated due to the retirement of the PI and the failure to establish an adequate control group for comparison purposes.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF RADIOLOGY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 93/119		<b>Status:</b> On-going	
<b>Title:</b> Gallbladder Ejection Fractions					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Dec 94		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John M. Bauman, MC					
<b>Associate Investigators:</b> MAJ Michael F. Lyons II, MC MAJ Richard R. Gomez, MC			Jerome Billingsley, M.D. LTC Clifford L. Simmang, MC		
<b>Key Words:</b> gallbladder, ejection fractions					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0		<b>OMA Cost:</b> \$6166.00		9/30/97	

Study Objective: To determine the clinical usefulness and reproducibility of gallbladder ejection fractions.

Technical Approach: Fifty volunteers will be studied on two occasions utilizing half of the normal radiopharmaceutical dose. These studies will be separated by no more than 30 days. Subjects will be given an injection of approximately 2.6 millicuries Tc-99m-DISIDA and serial one minute computer acquired images will be obtained for a maximum of 60 minutes. Once maximal gall bladder activity is achieved by visual inspection, 0.01 micrograms/kilo-gram sincalide will be given intravenously for three minutes via infusion pump. Serial one minute computer acquired images will be obtained for 30 minutes following this infusion. The results of the studies will not be used to determine patient care. The subject will be scheduled for cholecystectomy after the second DISIDA scan is completed. The gallbladder will be submitted to pathology for pathologic evaluation. The subject will complete a questionnaire prior to, and at one and six months post cholecystectomy. Mean, range, and standard deviation for each set of data will be calculated. A repeated measures ANOVA will be calculated.

Progress: 6 subjects were entered in FY 97, for a total of 24 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/077		<b>Status:</b> Terminated	
<b>Title:</b> Determination of Normal Regional Myocardial Thallium Distribution and Development of a New Display Technique					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Jul 94		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John M. Bauman, MC					
<b>Associate Investigators:</b> Jerome Billingsley, M.D.			COL Stanton R. Brown, MC James H. Timmons, MD		
<b>Key Words:</b> thallium, myocardial distaribution, new technique					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

**Study Objective:** (1) To determine the normal regional variation in the myocardial distribution of <sup>201</sup>Tl. (2) To use this information to create a color translation table for semiquantitative analysis of Thallium images. (3) To evaluate the ability of the new translation table to predict the presence or absence of significant coronary artery lesions at cardiac catheterization.

**Technical Approach:** We intend to pull all Thallium studies and cardiac catheterization data on patients who have had both studies at MAMC since 1 August, 1992. Results of Thallium and catheterization studies will be entered on worksheets and from there into a computerized database. We will review a minimum of 10 data sets where both the Thallium study and catheterization data are normal. The relative distribution of Thallium on the stress studies will be quantitated using a circumferential image profile on the short axis slices using 8 mid-ventricular slices which demonstrate a complete left ventricular chamber. Sixty values will be calculated for each of eight central stress slices. The maximum and minimum count values for all slices will give us the range of normal Thallium variation for each patient's stress study. This value, will be expressed as a percent of the maximum uptake. Finally the mean, range and standard deviation for the 10 patients' percent normal variations will be calculated. The color map will be created using the information from phase I. All images are limited to a maximum of 256 gray levels. We will divide these 156 levels into only 5 colors for our map. As a result, individual pixels will be colored according to their relative count value with respect to the maximum in the image. Break points for color levels will be determined by the mean percent normal variation and standard deviation. The new color translation will then be used to reinterpret a minimum of 50 Thallium studies for which cardiac catheterization data is available. Studies will be read separately by 2 board certified nuclear medicine physicians without knowledge of the clinical history, previous Thallium result, exercise data or catheterization result. Using only the new color table, results will be annotated as normal or abnormal. If abnormal, location and extent of abnormality will be recorded. Actual colors of defects will be recorded and subsequent data analysis for correlation with the bull's eye plots, prior image interpretations and cardiac cath data will be made for each color level of defect.

**Progress:** This study centered around a computer programming algorithm that was originally designed in 1994. Since that time, technology has replaced and made this original work obsolete in view of the rapid development of new computer tools and software. Therefore, the study was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/038	<b>Status:</b> On-going
<b>Title:</b> Digitally Acquired Radiographic Air Contrast Barium Enema vs. Colonoscopy in Polyp Detection, Cancer Detection, and cost in a Federal Tertiary Care Center		
<b>Start Date:</b> 12/17/93	<b>Est. Completion Date:</b> Jan 95	
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Gregory N. Bender, MC		
<b>Associate Investigators:</b> MAJ Michael F. Lyons II, MC		LTC Amy M. Tsuchida, MC CPT Thomas P. Peller, MC
<b>Key Words:</b> polyps, barium enema, colonoscopy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To determine if digitally acquired radiographic air contrast barium enema (DAR-ACBE) examinations of the colon might serve as a cost effective surrogate to colonoscopy in the MAMC colon cancer screening program.

**Technical Approach:** By obtaining DAR-ACBE and colonoscopy on the same patient a test of diagnostic equality for these two examinations will be performed. The diagnostic equality of these examinations will be tested by assessing their ability to find polyps >5mm in size and in finding cancers of any size.

**Progress:** Previously, as a pilot study, the investigators reviewed more than 1000 charts to determine the basic ability of DAR-ACBE to find polyps and cancer; approximately 800 were positive. However, no patients were entered. All the investigators, except for one, have been transferred to new duty stations, and there were no personnel in the Department of Radiology who were interested in performing the study. This investigator stated that she did not choose to become the principal investigator on the study. Therefore, it was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/034	<b>Status:</b> Completed
<b>Title:</b> Benign and Malignant Soft Tissue Tumors. Do Certain Tumors Tend to Occur in Certain Locations and Are Certain Tumors More Common in Certain Ages?		
<b>Start Date:</b> 02/21/97	<b>Est. Completion Date:</b> Jan 97	
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Lawrence M. Casha, MC		
<b>Associate Investigators:</b> Kransdorf MJ Rush A. Youngberg		
<b>Key Words:</b> Cancer:soft tissue, Cancer:location, Cancer:age		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: Formulate statistically a differential diagnosis based on Age and Anatomic Location that can help narrow the differential diagnosis of soft tissue tumor.

Technical Approach: The diseases which show statistical significance with P values of less than 0.05 will be used to create a differential diagnosis based on Age and Anatomic Location.

Progress: The findings show that certain benign and malignant soft tissue tumors have a propensity to occur in certain anatomic locations. The results were presented at the AMED Conference in Feb 97.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/081		<b>Status:</b> On-going	
<b>Title:</b> Pulmonary Manifestations of Gastro-esophageal Reflux Disease: HRCT Findings					
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Jan 96		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Manish K. Varma, MC					
<b>Associate Investigators:</b> MAJ Kazunori Yamamoto, MC			MAJ Cristopher A. Meyer, MC		
<b>Key Words:</b> GERD, HRCT, pulmonary					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** To investigate the pulmonary high resolution CT findings of patients with GERD. By categorizing HRCT findings in patients with GERD, a distinction may be made between pulmonary manifestations of GERD and other entities which often have similar plain film findings. This would allow clinical decisions regarding therapy, e.g. steroid therapy in UIP versus anti-reflux measurements to be facilitated.

**Technical Approach:** Gastroesophageal reflux disease is very common in Western Countries and is associated with significant morbidity. Based on symptoms alone, up to 44% of adult Americans experience GERD. The Gastroenterology Department has a proven population of patients with gastroesophageal reflux disease using the gold standard - 24 hour pH probe monitoring. 25 patients will be selected from the patient population after screening out those patients with prior lung disease, smoking, pregnancy, etc. that may interfere with pulmonary findings of GERD. High Resolution Computed Tomography of the lung will be performed in an attempt to categorized findings unique to GERD that are not discernible on plain film examination. CT and CXR findings will be reviewed by a radiologist and radiology resident. A grading system will be devised on the findings of the first five patients which will consist of five normal volunteers with normal pHs and no GERD. These findings will facilitate treatment options, e.g. steroid treatment in UIP verses anti-reflux precautions in GERD, in diseases that have similar plain film findings.

**Progress:** Three subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/166		<b>Status:</b> On-going	
<b>Title:</b> Cost Effectiveness of Early MRI in Traumatic Wrist Injury					
<b>Start Date:</b> 08/18/95			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard S. Makuch, MC					
<b>Associate Investigators:</b> LTC John M. Bauman, MC			Rush A. Youngberg CPT John D. Crocker, MC		
<b>Key Words:</b> Wrist, scintigraphy, cost effectiveness					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0	<b>Est. Accumulative</b> <b>OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

Study Objective: To determine the cost effectiveness and utility of scintigraphy in the management of patients with traumatic wrist injury whose initial radiographs are negative, yet who clinically are felt to have scaphoid fractures.

Technical Approach: This is a prospective blinded study to determine the cost effectiveness of a more accurate, slightly more expensive imaging modality in the management of patients with traumatic wrist injury. All patients over 18 years of age with a fall on the outstretched hand (a "FOOSH" injury) will be included. One hundred patients will be enrolled.

Those enrolled in the study will undergo a limited high resolution bone scan of each wrist (the uninjured wrist will serve as a comparison to the injured wrist) within 48-96 hours of the time of injury. When the clinician has determined that management is complete, the clinician will have access to the bone scan results, prior to the patients' discharge from care.

The radiographs will be reviewed by the chief of musculoskeletal radiology, the bone scans by a staff nuclear medicine physician, and the clinical evaluation and follow-up will be performed per usual orthopedic clinic practice at MAMC. Costs will be calculated based on the CHAMPUS allowable reimbursement for the services rendered as defined by the 1995 CPT codes of the American Medical Association. Data analysis will include determining if there is statistical significance between the costs of caring for clinically "false positive" fractures and the costs of early bone scintigraphy.

Progress: 11 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/046		<b>Status:</b> Completed	
<b>Title:</b> Intravenous Contrast-Enhanced MR Saline Arthrography: A Technique for Staging Juxta-articular Masses					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Liem T. Mansfield, MC					
<b>Associate Investigators:</b> LTC John D. Pitcher Jr., MC			Rush A. Youngberg		
<b>Key Words:</b> Arthrography:saline, juxta-articular masses					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To describe a new imaging technique for preoperative staging of juxta-articular masses

**Technical Approach:** 5 patients, requiring surgery for management of their tumors, were evaluated by CEMRSA as part of their diagnostic workup. These were patients who had juxta-articular neoplasms in whom neither physical examination nor conventional MR imaging determined if the adjacent joint was involved. The charts of these patients will be reviewed in order to correlate CEMRSA results with surgical and histologic staging. Accuracy of CEMRSA will be primarily determined by its ability to predict whether the synovium of the adjacent joint was invaded by neoplasm, since it is this criteria that determines if the joint can be salvaged. The results will be stated descriptively without data analysis.

**Progress:** Four subjects were studied. The investigators felt that the results indicated that IV contrast-enhanced MR saline arthrography was a good staging tool for juxta-articular masses. However, when the paper was submitted for publication, the reviewers wanted at least a couple of cases where the mass was actually in the joint. The Orthopedics Service at MAMC felt that they did not want to enter patients with joint involvement in the study. Therefore, no further work was done to obtain publishable results.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/027		<b>Status:</b> On-going	
<b>Title:</b> Helical Computed Tomography Oral Cholecystography (HCT-OCG) vs. Ultrasound (US) in the Detection of Cholelithiasis; Sensitivity, Specificity, and Cost					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Dec 98		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Robert E. Morgan, MC					
<b>Associate Investigators:</b> James H. Timmons, MD			LTC Gregory N. Bender, MC CPT Janice C. Stracener, MC		
<b>Key Words:</b> Cholelithiasis, HCT-OCG, ultrasound					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To identify the best methodology (HCT-OCG vs. US) for use in screening for the presence or absence of gallstones. Best, is defined as the examination with the greatest sensitivity, specificity and lowest cost.

**Technical Approach:** A prospective study in the identification of gallstones is to be completed comparing two imaging modalities in a large clinical study of 103 patients. The focus of the study is to identify which modality gives radiologists the greatest sensitivity and specificity in gallstone detection at the greatest economy. Surgery or overwhelming agreement among studies will provide the standard of truth. Chi-square analysis will be used to compare the results for statistical significance between the positive and negative rates as well as the average comparative cost.

**Progress:** 20 subjects were entered during FY 97, for a total of 24 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/076		<b>Status:</b> On-going	
<b>Title:</b> Effectiveness of Oral Dolasetron Mesylate (50 mg) versus Prochlorperazine in the Treatment of Nausea and Emesis Due to Fractionated Abdominal Radiotherapy					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark E. Shaves, MC					
<b>Associate Investigators:</b> LTC Kenneth A. Bertram, MC CPT Brent L. Kane, MC			LTC Steven S. Wilson, MC MAJ Nyun C. Han, MC		
<b>Key Words:</b> Nausea, emesis, abdominal radiotherapy, dolasetron mesylate, prochlorperaine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/21/97	

**Study Objective:** 1) To evaluate the effectiveness of dolasetron mesylate in the treatment of radiation-induced nausea and emesis (RINE) in patients undergoing fractionated abdominal radiotherapy. 2) To evaluate the safety and tolerability of oral dolasetron mesylate in cancer patients receiving radiotherapy. 3) To evaluate the net incremental health care resource utilization, and net incremental work productivity and family/household assistance associated with the use of dolasetron mesylate versus prochlorperazine in the treatment of RINE. 4) To evaluate the use of select quality of life domains in measuring quality of life in patients receiving treatment for RINE.

**Technical Approach:** This study is a randomized, double-blind, active-controlled, multi-center trial to evaluate the effectiveness and safety of oral dolasetron mesylate in patients exhibiting nausea or emesis after undergoing fractionated abdominal radiotherapy for malignant disease. Patients will be eligible for the study if they experience significant nausea requiring antiemetic medication or have had at least one emetic episode after receiving radiotherapy during the 5 day screening period. Patients will be randomized to receive either oral dolasetron mesylate 50 mg qd or prochlorperazine 10 mg tid. Study medications will be ingested on a tid schedule. Patients randomized to dolasetron mesylate will take one 50 mg dolasetron mesylate capsule (as their first dose) and two matching placebo capsules for a total of three daily doses. The first daily dose of study medications will be ingested within 1 hour prior to the start of radiotherapy. The second and third daily tid scheduled doses of study medication (placebo or prochlorperazine) will be ingested over the remaining 24 hour treatment day. For each day on which no radiotherapy is administered (eg, weekends), study drug is to be administered using the same regimen (1 capsule tid). Radiation treatment will be administered for a minimum of 5 and a maximum of 30 days during the treatment phase. Study drug may be continued for up to 3 days after completion of the last fraction of radiotherapy.

**Progress:** Protocol was suspended in Mar 97 due to problems with the formulation of the drug. It was reopened in Apr 97 after problems were worked out. No subjects have been entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/043	<b>Status:</b> Terminated
<b>Title:</b> Comparison of CO <sub>2</sub> , Water Soluble Contrast, and Water Soluble Contrast with Methyl-Cellulose During Computed Tomographic Enteroclysis Using a Porcine Model		
<b>Start Date:</b> 12/19/96	<b>Est. Completion Date:</b>	
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> James H. Timmons, MD		
<b>Associate Investigators:</b> LTC William C. Williard, III, MC		LTC Gregory N. Bender, MC
<b>Key Words:</b> CT-Enteroclysis, porcine, carbon dioxide, water soluble contrast, methyl-cellulose, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To identify the best contrast agent for use in the CT evaluation of small bowel masses and partial small bowel obstruction while using CT-enteroclysis methodology.

Technical Approach: Following successful performance of the surgical procedures, and helical CT image production, the following approach to data analysis is outlined. Initially two radiologists, blinded to the surgical information, will read the CT examinations from a digital monitor under similar ergonomic conditions. They will not be confined to certain window/level settings or use of specific electronic tools. All examinations will be randomly mixed and numbered within contrast groups. The reading of the studies from different contrast groups will be separated by at least a 2 week time frame. There will be 3 outcome measures; 1) site of obstruction; 2) # of beads; and 3) size of beads. The outcome measures will be expressed as a score relative to the correct state. This is straightforward for the number of beads; e.g. if 5 beads were planted and 4 were detected, the score would be 4/5 as the number of beads missed should not covary with the number of beads placed. This data would be analyzed using a repeated measures analysis of variance (ANOVA). The initial power analysis was based on Chi squared analysis made of the categorical data which will be ongoing throughout the study to determine the potential for an early termination of the study if sufficient data has been collected. A similar study with RVES will be performed and compared to the CT-E data using Chi squared analysis and surgical data for the standard of truth.

Progress: The principal investigator on this protocol was changed to Dr. James Timmons in Sep 97 after the departure of Dr. Greg Bender. A pilot study was done of the technical feasibility of the visibility of the CT markers. After careful consideration, Dr. Timmons determined that he would not be adequately resourced to pursue this investigation.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/142		<b>Status:</b> On-going	
<b>Title:</b> Radiologic Guided Aspiration of Intra-articular Ganglia in the Knee					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Manish K. Varma, MC					
<b>Associate Investigators:</b> LTC John D. Pitcher Jr., MC			Rush A. Youngberg		
<b>Key Words:</b> Knee:ganglion, aspiration					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine whether radiologic guided aspiration and subsequent injection of 1% Xylocaine of intra-articular ganglia in the knee is a feasible alternative to arthroscopic excision.

**Technical Approach:** Intra-articular ganglia in the knee are an uncommon cause of knee pain. Patients with intra-articular ganglia in the knee had good or excellent results with arthroscopic excision of the ganglia. However, 50% to 78% of these patients had no associated internal derangement. CT guided aspiration of intra-articular ganglia in the knee has been successful. Ultrasound guided aspiration of ganglion cysts is a potentially cost effective alternative to surgery. We propose to perform radiologic guided aspiration of 15 patients with intra-articular ganglia in the knee. These patients have knee pain and intra-articular ganglia in the knee demonstrated on MRI. All patients will be followed at 3 month and 6 month after the procedure. An MRI will be obtained immediately post-procedure and at 6 months follow up. Failures will be offered operative (arthroscopy) treatment. The standard treatment (arthroscopy) who do not opt for aspiration. We will determine whether the intra-articular ganglia in the knee is the cause of the patients' symptom. Also, we will show whether aspiration and injection of 1% Xylocaine will successfully remove the ganglion cysts.

**Progress:** 3 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/045		<b>Status:</b> Completed	
<b>Title:</b> Comparison of CT-Enteroclysis and Traditional CT in the Setting of Suspected Partial Small Bowel Obstruction					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Daniel W. Walsh, MC					
<b>Associate Investigators:</b>			LTC Gregory N. Bender, MC		
<b>Key Words:</b> CT-Enteroclysis, small bowel:obstruction					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** Retrospective study comparing traditional abdominal/pelvic CT to CT-Enteroclysis (CT-E) in evaluating patients suspected of partial small bowel obstruction. Only patients with both studies performed during the same clinical episode will be included. Surgical and chart review will be performed to evaluate the sensitivity/specificity of each procedure. Chart review will also be performed to identify any group of patients which may benefit from having CT-Enteroclysis as the front-line examination.

**Technical Approach:** One hundred fifty patients with CT-E examinations performed for suspected partial SBO over a three year period were reviewed for a companion traditional CT obtained during the same clinical episode. Chart review and surgery were used as gold standards for determining sensitivities and specificities of the two methodologies. A chart review was also performed to identify any referral categories which may benefit from one method over the other.

Thirty-three CT-E examinations had a companion CT during the same clinical episode. Two major referral categories were identified: (1) patients with a history of benign medical or surgical disease (n=20), and (2) patients with a history of malignancy or symptoms suspicious for malignancy (n=13). Inpatients with malignancy, CT-E was found to be superior to CT in identifying partial SBO, and in identifying or excluding intraluminal/mural disease.

In the setting of malignancy, CT-E was superior to CT in patients with suspected partial SBO. CT-E may be the first-line imaging modality in these patients, strengthening one's final CT conclusions and obviating the need for additional studies.

**Progress:** 36 patients with CT-E examinations performed for suspected partial SBO over a three year period and also a companion traditional CT obtained during the same clinical episode were studied. In patients with malignancy, CT-E was found to be superior to CT in identifying partial SBO, and in identifying or excluding intraluminal/intramural disease. CT-E may be the first line imaging modality in these patients, strengthening the final CT conclusions and obviating the need for additional studies. A prospective study comparing the two methodologies is warranted in patients with suspected partial SBO.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/023		<b>Status:</b> Terminated	
<b>Title:</b> Validation of Nipple Arc Lesion Localization Technique					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Radiology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Malcolm A. Whitaker, MC					
<b>Associate Investigators:</b> MAJ Donald V. Smith, MC			LTC Jeffery C. Morissette, MC, USN		
<b>Key Words:</b> Breast:cancer, nipple-arc-technique					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

Study Objective: Construct a computer mathematical breast model and with subsequent computer manipulation, test the validity or failure of the previously described "nipple ARC technique" which is currently used to localize breast lesions between the medial-lateral oblique mammography view and the cranial-causal mammography view.

Technical Approach: Surface measurements of breasts prior to and during standard compression will be obtained and utilized to construct a generic mathematical breast model which can be manipulated in virtual space. Once constructed, the mathematical breast model can be used to test many commonly used lesion localization techniques/methods to determine their validity. The breast measurements will be obtained during routinely scheduled mammograms at MAMC. The measurement process is estimated to add approximately 5 minutes to each of the 60 planned exams. No additional radiation is needed/required. No invasive actions are needed.

Progress: Ten subjects were entered before the PI received orders assigning him to DACH. Since the data were inadequate for significant analysis, the protocol was terminated at MAMC. The PI hopes to continue the protocol at DACH.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY,  
CARDIOTHORACIC SURGERY SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/156		<b>Status:</b> Terminated	
<b>Title:</b> North American Duraflo II Working Group					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Cardiothoracic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Blaine R. Heric, MC					
<b>Associate Investigators:</b>			LTC Maceo Braxton Jr, MC		
<b>Key Words:</b> Duroflo II, heparin, cardiopulmonary bypass circuits					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		02/21/97

**Study Objective:** To determine if Duraflo II, (a heparin surface treatment) creates in a controlled, prospective, randomized study, a more biocompatible extracorporeal environment as evidenced by the following key patient outcomes indices: (1) homologous transfusion requirements (2) post-op hours until extubation (3) post-op hours until SICU discharge (4) post-op days until hospital discharge.

**Technical Approach:** The deleterious effects of cardiopulmonary bypass on hematologic parameters have been well established in cardiac surgery. In particular, the systemic inflammatory response is a well recognized entity which occasionally may create severe clinical problems including ARDS (Adult Respiratory Distress Syndrome), neurologic dysfunction, myocardial edema and myocardial dysfunction, and postoperative weight gain.

Heparin coating all blood containing surfaces of the extracorporeal circuit creates a "pseudo endothelium". Early studies, in a relatively small number of patient in Europe, have indicated that platelet function and numbers are preserved. Bleeding is decreased. Levels of complement activation are reduced and, therefore, postoperative pulmonary function is improved. The number of patients studied in a randomized blinded fashion, however, has been very small and, therefore, improved clinical outcome using this new technology has not been documented.

The Duraflo tubing is one of several heparin coated or "biocompatible" surfaces which have been the focus of active research by many of the industries in the past several years. No U.S. center has reported a clinical evaluation of the product, despite the fact that the FDA has approved the majority of the components for use in routine clinical practice. Adding the heparin coating to the tubing increases the expense of open-heart surgery and no study has yet been able to justify its use. This will be the first study to address this question in a scientific fashion.

**Progress:** This multicenter study was terminated at MAMC when the principal investigator was transferred. Eighty-three subjects were entered with no adverse events.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY,  
GENERAL SURGERY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/108		<b>Status:</b> Completed	
<b>Title:</b> Telomerase Activity and Expression of p53, DCC, and Rb in Human Colorectal Cancer					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
LTC William C. Williard, III, MC			MAJ Raymond S. Lance, MC		
MAJ Kenneth W. Westphal, MC			Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer: colorectal, telomerase activity, temomere length					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in colorectal tumor tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of colorectal cancer.

**Technical Approach:** Tissue samples will be taken from 35 male and female patients undergoing surgical resection for colorectal cancer. All malignant and benign tumors of the colon and rectum found during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress:** Telomerase activity was found to be present in a significant number of colorectal carcinomas as compared to the normal adjacent tissue. The presence of telomerase activity in both early and late stage tumors supports the concept that telomerase activation is an early event in the malignant process. p53 mutations, although present in the majority of tumors studied, did not correlate significantly with telomerase activity levels or tumor staging.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/106		<b>Status:</b> Terminated	
<b>Title:</b> Telomerase Activity and Telomere Length in Human Breast Cancer					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>			CPT Wade K. Aldous, MS		
LTC William C. Williard, III, MC			MAJ Raymond S. Lance, MC		
MAJ Kenneth W. Westphal, MC			Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer:breast, telomerase acitivity, telomere length					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous breast tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of breast cancer.

**Technical Approach:** Tissue samples will be taken from 50 female and male patients undergoing surgical resection for breast cancer. All malignant and benign tumors resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress:** This study was terminated because the investigators were unable to harvest breast tissue due to the small size of the breast tumors and the potential interference with determination of surgical margins.

### Detail Summary Sheet

**Date:** 30 Sep 97                      **Protocol No.:** 97/064                      **Status:** On-going

**Title:** Prognostic Significance of p53 Mutations in the Lymph Nodes of Dukes B  
Colon Cancer Patients

**Start Date:** 04/18/97                      **Est. Completion Date:** Jun 97

**Department:** Surgery/General                      **Facility:** MAMC

**Principal Investigator:** CPT Tommy A. Brown, MC

**Associate Investigators:**  
CPT Wade K. Aldous, MS                      MAJ Kenneth S. Azarow, MC  
LTC William C. Williard, III, MC                      LTC Jerome B. Myers, MC

**Key Words:** Cancer:Dukes B colon, lymph nodes, p53 mutations

Accumulative	Est. Accumulative	Periodic Review:
MEDCASE Cost:	OMA Cost:	
\$0	\$0.00	9/30/97

**Study Objective:** Our objective is to evaluate the relationship between p53 mutations in the lymph nodes and long term survival of patients with colon cancer.

**Technical Approach:** This is a retrospective pathology review and chart review. Slides of lymph nodes from 50 Dukes B colon cancer patients will be stained for p53 mutation using standard immunohistochemical stains. These results will be compared to long term tumor recurrence patterns.

**Progress:** 20 subjects have been entered in FY 97, for a total of 35 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/141		<b>Status:</b> On-going	
<b>Title:</b> A Prospective Multi-institutional Study to Determine the Sensitivity and Specificity of Telomerase in ERCP Brushings for Detection of Pancreatic and Biliary Cancer					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>			MAJ Kenneth S. Azarow, MC		
LTC William C. Williard, III, MC			CPT Wade K. Aldous, MS		
LTC Amy M. Tsuchida, MC			Thegerge MM		
Kavolius J			North J		
Martin T			Setz S		
<b>Key Words:</b> Cancer:pancreatic, Cancer:biliary, telomerase					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>9/30/97</b>

**Study Objective:** To evaluate telomerase activity as a screening modality for the detection of pancreatic and biliary tumors.

**Technical Approach:** This study is designed to evaluate the efficacy of measuring telomerase activity in endoscopic retrograde cholangiopancreatography (ERCP) brushings and bile samples as screening tool for pancreatic carcinoma and cholangiocarcinoma. The six Army medical centers involved include MAMC, WRAMC, TAMC, DDEAMC, WBAMC and BAMC. Patients with suspicious pancreatic or bile duct lesions will have lumen brushings of the lesions and bile collected and shipped to MAMC to determine if telomerase activity is present in the specimens. Additionally, after surgical excision of the suspicious lesions, a sample of the primary tumor will also be sent to MAMC for evaluation of telomerase activity. The results of these tests as well as patient clinical data will be analyzed to determine the sensitivity and predictive value of telomerase as a screening tool for pancreatic and bile duct malignancy. We estimate the total number of patients needed to complete the study to be 36 for each of the two groups utilizing a power analysis. The data will be collected and analyzed using statistical software to evaluate surgical correlation of telomerase activity in ERCP brushings and bile fluid. Major analysis being the correlation of the surgical results to the telomerase activity detected in FNAs, reporting sensitivity and specificity, along with positive and negative predictive value. The study will run for approximately 1 year. Consent is required for ERCP brushings for all patients.

**Progress:** This new study has not been started.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/143		<b>Status:</b> On-going	
<b>Title:</b> A Prospective Multi-institutional Study to Determine the Sensitivity and Specificity of Telomerase in Thyroid FNAs for the Detection of Thyroid Cancer					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC					
<b>Associate Investigators:</b>					
LTC William C. Williard, III, MC		MAJ Kenneth S. Azarow, MC			
CPT Wade K. Aldous, MS		MAJ Clifford A. Porter, MC			
MAJ Raymond S. Lance, MC		CPT Brenda K. Bell, MC			
Thegerge MM		CPT Janice C. Stracener, MC			
North J		Kavolius J			
		Martin T			
<b>Key Words:</b> Cancer:thyroid, telomerase, FNA					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** Our objective is to evaluate telomerase activity in thyroid fine needle aspirations as a screening modality for the detection of thyroid cancer.

**Technical Approach:** This study is designed to evaluate the efficacy of measuring telomerase activity in fine needle aspirations of thyroid nodules as a screening tool for thyroid carcinoma. The six Army medical centers involved include MAMC, WRAMC, TAMC, DDEAMC, WBAMC and BAMC. Patients with suspicious thyroid nodules requiring fine needle aspiration (FNA) will have additional FNA samples taken at the time of surgery sent to MAMC to determine if telomerase activity is present in the specimens. Additionally, after surgical excision of the thyroid, a sample of the primary tumor will also be sent to MAMC for evaluation of telomerase activity. The results of these tests as well as patient clinical data will be analyzed to determine the sensitivity and predictive value of telomerase as a screening tool for thyroid malignancy. We estimate the total number of patients needed to complete the study to be 360 utilizing a power analysis. The total number of specimens analyzed will be approximately 1000. The data will be collected and analyzed using statistical software to evaluate surgical correlation to telomerase activity in FNAs. Major analysis being the correlation of the biopsy cytology to the telomerase activity detectability, reporting sensitivity and specificity, along with positive and negative predictive value. The study will run for approximately one year. Consent is required for additional FNA passes for all patients.

**Progress:** This new study has not been started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/009		<b>Status:</b> On-going
<b>Title:</b> Postoperative Cisapride Therapy After Colorectal Surgery				
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Feb 98	
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Tommy A. Brown, MC				
<b>Associate Investigators:</b> CPT Jerome M. McDonald, MC			LTC William C. Williard, III, MC LTC Gregory N. Bender, MC	
<b>Key Words:</b> Surgery:colorectal, cisapride				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: To test the efficacy of cisapride in the postoperative period in relation to bowel motility and length of hospital stay.

Technical Approach: In this double-blind study 66 patients undergoing colorectal surgery will be randomly assigned to one of two groups. The experimental group will receive 20mg cisapride orally four times daily until discharged; the control group will receive placebo. All patients will be given an oral sitz mark radiographic marker on the first postoperative morning to follow bowel motility. A daily portable abdominal x-ray will be taken until 80% of the sitz markers have completely passed through the system. Length of hospital stay, daily progression of radiographic marker, onset of bowel movements, regular diet intake and perioperative complications will be monitored and compared for experimental and control groups.

Progress: 20 subjects were entered in FY 97, for a total of 40 subjects. Study will be completed by Feb 98.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/047		<b>Status:</b> On-going	
<b>Title:</b> Genetic Testing for Inherited Cancer					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Sep 97		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> Preston L. Carter, M.D.					
<b>Associate Investigators:</b> Charlene P. Holt, M.D.			Jamilyn L. Daniels, M.S., C.G.C.		
<b>Key Words:</b> Cancer:breast, genetics, BRCA1, BRCA2, predisposition testing					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** We propose to develop a model for genetic counseling and testing for patients at risk for breast cancer. Multiple phases of a program will be developed and tested in this pilot program at Madigan. Two breast cancer susceptibility genes will be studied, BRCA1 and BRCA2. A commercial laboratory will be used to perform the actual testing. Results and interpretation of each patient's test will be sent to Madigan, and each patient enrolled in appropriate counseling and medical care.

**Technical Approach:** Historical data indicate that 55 of 100 patients meeting the inclusion criteria may test positive for BRCA1 or BRCA2 genetic mutations. Thus we anticipate that approximately 23 patients from the group of 50 recruited at Madigan will have a positive test result and request additional care. Informed consent will be performed at two points in the project, first before patients complete a questionnaire, perform pre-test counseling and education, and second before providing a blood sample for genetic testing. The guidelines for follow-up of individuals testing positive for BRCA1 or BRCA2 genetic mutations have been presented by Dr. Wylie Burke to the National Cancer for Human Genome Research Advisory Council. Madigan patients will be instructed and counseled on their individual test results and choices of action for the follow-up surveillance.

**Progress:** 51 subjects have been enrolled. Two abstracts have been published and a presentation was made at the DOD Breast Cancer Conference.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/119		<b>Status:</b> Completed	
<b>Title:</b> C-Reactive Protein in the Diagnosis of Acute Appendicitis					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Apr 95		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Mathew H. Chung, MC					
<b>Associate Investigators:</b> CPT Donald G. Kim, MC			CPT Brad J. Davis, MC LTC William C. Williard, III, MC		
<b>Key Words:</b> Appendicitis, C-reactive protein					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine the negative predictive value of C-reactive protein (CRP) in an attempt to determine if the negative exploratory laparotomy rate (30%) can be significantly reduced. A secondary objective would be to calculate the cost savings of reducing the negative exploratory laparotomy rate.

**Technical Approach:** This study will attempt to better define the role, if any, of measuring CRP level in the diagnosis of acute appendicitis. It will determine if a normal CRP is a better negative predictor of appendicitis than normal serial leukocyte counts (WBC) and erythrocyte sedimentation rate (ESR). This study will include 100 subjects, 18 years and older, identified by the general surgery service with suspected appendicitis. Patients will have CRP, ESR and WBC testing during initial evaluation as routine. Those who do not undergo immediate surgery will have CRP, ESR and WBC tested again 12 hours later. The levels of CRP at both of these times and the need for surgery will be collected as data. Those who do not eventually go to surgery will be considered to have no appendicitis for data analysis.

**Progress:** 20 were entered and data analysis is in progress. The PI has been reassigned to Ft. Stewart, GA. After data analysis is complete, the PI will attempt to enter more patients at Ft. Stewart if more are needed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/045		<b>Status:</b> Suspended	
<b>Title:</b> The Effect of Low-Dose Dopamine on Splanchnic Blood Flow with Intra-abdominal Hypertension in Domestic Yorkshire Swine, <i>Sus scrofa</i>					
<b>Start Date:</b> 01/19/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Mathew H. Chung, MC					
<b>Associate Investigators:</b>			LTC Patrick J. Offner, MC		
<b>Key Words:</b> Hypertension, blood flow, dopamine, swine,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

Study Objective: To investigate the ability of low-dose dopamine to improve visceral blood flow and organ perfusion during induced intro-abdominal hypertension.

Technical Approach: We will use an established porcine model of elevated intra-abdominal pressure. The animals will be anesthetized, mechanically ventilated and instrumented. Femoral arterial and venous catheters will be placed and a Swan-Ganz pulmonary artery catheter will be placed via jugular vein. Laparotomy will be performed for the placement of Doppler flow probes and gastric and ileal tonometers. Two catheters will be placed in the abdominal cavity percutaneously and a urinary catheter will be placed through a cystotomy. Following instrumentation, animals will be randomly assigned to one of four experimental groups. Group I is the negative control with no further manipulations. Group II will have elevated intra-abdominal pressure by instillation of saline solution. Group III will have the same elevated (Group II) intra-abdominal pressure established plus low dose dopamine. Group IV will have low-dose dopamine alone. There will be six animals per group. Intra-abdominal pressures of 20 and 40 mm Hg will be studied. Measurements will include the following every 20 minutes for two hours during the experiment: (1) renal, hepatic, and superior mesenteric arterial flow and portal vein flow, (2) hepatic and renal perfusion, (3) gastric and terminal ileum pH, (4) cardiac hemodynamics, and (5) laboratory values on ABG, mixed venous blood gas and lactate levels.

Progress: Suspended Jul 97 due to the PCS of the PI. Department of Surgery has requested that the protocol be left in a suspended status until a new PI can take over.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/038		<b>Status:</b> On-going	
<b>Title:</b> Advanced Trauma Life Support Course Utilizing the Goat (Capra hircus)					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL William E. Eggebrotten, MC					
<b>Associate Investigators:</b>			MAJ Katherine L. Bevill, MC		
Preston L. Carter, M.D.			CPT Ronald J. Place, MC		
LTC Clifford L. Simmang, MC			LTC Patrick J. Offner, MC		
<b>Key Words:</b> Training protocol:goat, ATLS,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					07/18/97

Study Objective: The objective of this training exercise is to teach physicians one safe method of performing five life-saving procedures for trauma patients.

Technical Approach: This training exercise will MAMC residents in the initial management of trauma patients. The physicians will practice the safe methods of performing the following life-saving procedures in the order listed: venous cut down, dagnostic peritoneal lavage, chest tube insertion, pericardiocentesis and cricothyroidotomy. The procedures will be performed after the animals are properly prepared and adequately anesthetized for surgery. The endpoint of this training will be completion of all procedures or evidence of excessive duress or anesthetic instability. Students will be evaluated by instructors on the direct basis of psychomotor skills and verbalization of the indications, contraindications and potential complication of each procedure.

Progress: 6 subjects where trained during FY 97, for a total of 48 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/035		<b>Status:</b> On-going	
<b>Title:</b> Madigan Army Medical Center Institute for Advanced Endoscopic Training Using the Pig (Sus scrofa)					
<b>Start Date:</b> 01/23/95			<b>Est. Completion Date:</b> Jan 98		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL William E. Eggebroten, MC					
<b>Associate Investigators:</b>			LTC William C. Williard, III, MC		
CPT Donald G. Kim, MC			MAJ Clifford A. Porter, MC		
MAJ David M. Watts, MC			LTC Patrick J. Offner, MC		
LTC Clifford L. Simmang, MC			MAJ Timothy F. Deaconson, MC		
<b>Key Words:</b> Training:endoscopic, pig,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0		<b>OMA Cost:</b> \$0.00		07/18/97	

**Study Objective:** To familiarize General Surgery residents, staff, and invited surgeons from our local community with techniques in the management of advanced endoscopic-laparoscopic techniques. This would familiarize surgeons with techniques for laparoscopic procedures upon the esophagus and stomach, especially for anti-reflux procedures, and the biliary tract for cholecystectomy and common bile duct exploration and for the small intestine in colon for intestinal resection, appendectomy, and colonic resection.

**Technical Approach:** This training protocol on laparoscopic and endoscopic surgical procedures will use a total of 10 pigs. Two to four pigs will be used per session with three sessions per year. The animals will be maintained on a nothing-by-mouth status for 12 hours prior to the procedures. General anesthesia will be used. The animals will be intubated, prepped and maintained on inhalant anesthesia. At the completion of the procedures, the pig will be euthanized. During each procedure, each animal will be used for a single training episode. Maximum teaching benefit will be obtained by repeating the procedures in order that each trainee assigned to the animal may have an opportunity to perform the procedure in rotation. Critique forms will be utilized for the training and will provide evaluation of effectiveness of the course.

**Progress:** 2 subjects were trained during FY 97, for a total of 16 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/022		<b>Status:</b> On-going	
<b>Title:</b> The Use of Autologous Fibrin Glue to Prevent Post-operative Seromas in Patients Undergoing modified Radical Mastectomy					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Bret R. Hansen, MC					
<b>Associate Investigators:</b> CPT Daniel D. Mais, MC			LTC Patrick J. Offner, MC		
<b>Key Words:</b> Mastectomy, seroma, fibrin glue					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine if the use of autologously donated fibrin glue can decrease the incidence of post-operative fluid collections in patients undergoing modified radical mastectomy.

**Technical Approach:** We plan to conduct a prospective, randomized study evaluating the effects of autologously donated fibrin glue on the flaps created during modified radical mastectomy in attempts to increase the adhesion of the flaps to the underlying tissue and prevent post-operative fluid collections. A total of 60 subjects will be recruited and randomized to a study group and a control group. All subjects will donate one unit of autologous blood pre-operatively. This blood will be used to provide the autologous fibrinogen for the study group. Surgeons will be given the fibrin preparation or saline to apply after mastectomy. The surgeons will be blinded as to whether they are applying fibrin glue or control saline. Drainage from the surgical area will be recorded by the subjects and a blinded evaluator will assess fluid accumulation at least weekly after drains are removed. Seroma fluids will be drained as necessary. Rates of seroma formation will be compared using chi-square analysis. The mean total amount of drain output and the mean length of time for the drains to be discontinued will also be analyzed using the Student's T-test or a non-parametric test should the distribution prove to be non-Gaussian.

**Progress:** No subjects were entered during FY 97.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/099		<b>Status:</b> Terminated	
<b>Title:</b> Evaluation of Multiple Metastatic Tumor Sources for Mutation of Human Metastasis Suppressor Gene KAI1					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Jerome M. McDonald, MC					
<b>Associate Investigators:</b> LTC William C. Williard, III, MC CPT Jason L. Blaser, MS			MAJ Raymond S. Lance, MC Katherine H. Moore, Ph.D.		
<b>Key Words:</b> Cancer:bladder, Cancer:breast, Cancer:colon, Cancer:kidney, Cancer:lung, Gene KAI1					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The objective is to demonstrate a loss of expression in the recently localized prostate cancer metastasis suppressor gene, KAI1, in metastatic bladder, breast, colon, kidney, and lung carcinoma.

**Technical Approach:** The study is designed to determine the presence or absence of the KAI1 metastasis suppressor gene in histologically confirmed metastatic bladder, breast, colon, kidney, and lung carcinoma. KAI1 has been shown to be present in nearly all human tissues to include colon, breast, lung, and kidney by Dong, et al. and is felt to code for an intercellular adhesion molecule. Reverse Transcriptase polymerase chain reaction will be used to amplify the extracted KAI1 RNA from paraffin blocks of histologically confirmed malignant tissue with histologic confirmation of metastasis. Because clinical follow-up is available on all patients in the Tumor registry, patient follow-up can be monitored. The sample population will include any specimen sent to Madigan Army Medical Center's Department of Pathology with histologic confirmation of malignancy by the Madigan Army Medical Center Department of Pathology or an outside institution at pathology's request with histologic confirmation of metastasis. Direct invasion of adjacent tissues by local growth or lymph node involvement does not constitute metastasis for purposes of this study. Sample size will include 10 species for each study organ. All histologic types and grades will be acceptable for analysis.

**Progress:** No patients were entered in this study before a study was published with approximately 10 times the number of specimens and more types of specimens. Therefore, the study was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/148		<b>Status:</b> Completed
<b>Title:</b> Outcomes of Varicocele Ligation Done For Pain: A Chart Review				
<b>Start Date:</b> 06/20/97		<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery/General		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Andrew C. Peterson, MC				
<b>Associate Investigators:</b> MAJ Henry E. Ruiz, MC		MAJ Raymond S. Lance, MC		
<b>Key Words:</b> Varicocele, ligation, pain				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

Study Objective: To determine outcomes of surgical repair of scrotal varicoceles done for pain by assessing patient satisfaction by telephone interview.

Technical Approach: This study will consist of two phases. Phase I: A comprehensive chart review will first be done. Data recorded will include address, SSN, age, race and reason for seeking medical attention such as pain, infertility, atrophic testicle. Phase II: Telephone interviews will then be conducted with each patient who's chart is reviewed. Questions will be asked relating to resolution of pain, complications of surgical management and patient conclusions about the procedure such as would they have it done again. DEERS will be use for those patients not reachable by telephone listings available in CHCS and patient charts. The data will then be analyzed using descriptive statistics.

Progress: Fifty-eight subjects were entered; 35 subjects finished the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/142		<b>Status:</b> Terminated	
<b>Title:</b> Development of An Animal Model for a Simple Bone Cyst in the Goat					
<b>Start Date:</b> 05/26/95			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard C. Rooney, MC					
<b>Associate Investigators:</b>			LTC John D. Pitcher Jr., MC		
<b>Key Words:</b> Cyst:bone, goat model,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					06/21/96

**Study Objective:** Our primary objective is to devise an animal model to observe the developmental course of a simple bone cyst. We will use a goat (*Capra hircus*) as our model for the human system.

**Technical Approach:** We propose to develop an animal model and study the developmental course of a simple bone cyst. Since the lining of a simple cyst is similar to the joint lining of synovial tissue, we will test the hypothesis that the intraoperative implantation of synovium will develop into a cyst. Since human bone cysts are often cryptic until a fracture or other symptom occurs, they are not well studied. The development of such a model should facilitate many potential studies of simple bone cysts. Pre-operatively, the goats will undergo a baseline radiographic appraisal of the limbs. Five young animals less than two months old will be used to simulate a fetus when the aberrant synovial implantation of tissues is thought to occur. Under general anesthesia, a partial synovectomy will arthroscopically performed on the hip with implantation made on an adjacent bone. Post-operatively, the goats will be radiographed to appraise maturation of the bone cyst over a twenty three month period. The goats will then be euthanitized and their cyst lining analyzed and compared to that of synovium. Radiographs will be assessed by clinical means to determine development of a unicameral bone cyst. All data will be evaluated for the feasibility of the model.

**Progress:** This study was terminated because the PI was transferred to Alaska and the funding was not approved.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/141		<b>Status:</b> Suspended
<b>Title:</b> Development of a Pig Model to Produce a Growing Fused Limb by Transferring Half of the Open Growth Plate From the Lower End of the Femur to the Upper End of the Tibia When the Tibia's Growth Plate....				
<b>Start Date:</b> 05/26/95		<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery/General		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Richard C. Rooney, MC				
<b>Associate Investigators:</b> LCDR Dave Sitler, MC		LTC John D. Pitcher Jr., MC		
<b>Key Words:</b> Arthrodesis, hemi-femoral turndown, tibial replacement,Animal Study				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		06/21/96

Study Objective: Our primary objective is to determine the feasibility of maintaining open physal plates in an autogenous, vascularized bone graft that has been traumatized by operative relocation. We will use a pig as our model for the human system in this pilot study.

Technical Approach: Research has indicated that it is possible to split the lower end of the adult femur (thigh bone), leave its vascular (blood) supply intact, and flip it upside down in order to use it as a replacement for the upper end of the tibia. We intend to develop a similar procedure in skeletally immature pigs to permit the limb to continue its normal growth while in a fused position. The technique is illustrated in the protocol. The total amount to limb growth should be normal because the growth plate is still functional at both ends of the femur. Before the procedure, the pigs will be weighed, have arteriograms and X-rays of limbs taken for status and measurement, establishing a baseline limb length. The some procedures will be performed at one, six and eleven months to assess bone growth. The animal will then be euthanitized and histologically examined. Radiographs, arteriograms, an limb length measurements will be evaluated by standard clinical means. Lengths of limbs will be measured and contralateral joints will be examined and compared to the surgical plates. The operative and non-operative limbs will be compared for parallel slopes.

Progress: This protocol was suspended when the principal investigator was reassigned in FY 96. It will remain in a suspended status until a new PI is approved and it has been rereviewed by the LACUC as stated in the minutes when it was approved.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/184		<b>Status:</b> Terminated	
<b>Title:</b> A Phase II Study to Evaluate LY320052 (rHbl.1) Compared to Standard Allogeneic Blood Transfusion Therapy in Elective Surgery					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Nov 96		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ David M. Watts, MC					
<b>Associate Investigators:</b>			LTC William C. Williard, III, MC		
Preston L. Carter, M.D.			LTC Patrick J. Offner, MC		
MAJ Clifford A. Porter, MC			MAJ Timothy F. Deaconson, MC		
COL William E. Eggebroten, MC					
<b>Key Words:</b> Transfusion therapy, LY320052 (rHbl.1), allogeneic blood therapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					10/18/96

**Study Objective:** The objective of this study is to examine the efficacy of rHb1.1 (LY320052) as a hemoglobin-based oxygen carrier (HBOC) and colloid volume expander in patients undergoing elective surgery. The primary efficacy objective is to determine whether administration of rHb1.1 reduces the proportion of patients undergoing elective surgery who receive an allogeneic blood transfusion intra-operatively or post-operatively through 7 days post surgery. Another objective is to determine the safety of rHb1.1 compared with standard transfusion therapy.

**Technical Approach:** This is a multi-center, randomized, double-blind, active-controlled, parallel study of approximately 192 patients. Standard therapy of allogeneic blood transfusion will be used as the active control. Patients between the ages of 18 and 75 who are ASA I, II or III undergoing elective surgery with an anticipated intraoperative blood requirement of 2 to 4 units will be considered for this study. After obtaining consent, patients will be screened with a history, physical examination, and laboratory evaluation. Monitoring and data collection for this study will include pre-, intra-, and post-operative vital signs, and hemodynamic monitoring. Patients will be randomly assigned to receive either standard allogeneic transfusion or rHb1.1. Allogeneic transfusions will be packed red blood cells only, not whole blood. Patients randomized to the standard transfusion group will receive as many allogeneic units as is appropriate and those patients randomized to the rHb1.1 group may receive from 1 to up to 4 units of rHb1.1.1, but anything necessary over 4 will be met with standard therapy. Patients will be followed during and after surgery with examinations and blood tests at days 1, 2, 7, and 28 post surgery. Efficacy will be analyzed by measuring the number of allogeneic units after surgery for each group, the average comparative numbers of rHb1.1 units compared to standard therapy. The Lilly Statistical and Mathematic Science Department will perform the statistical analysis presented in the final report.

**Progress:** Lilly (the sponsor) reported adverse liver and cardiac toxicology results in cynomolgus monkeys exposed to rHb1.1. This project was then terminated in Mar 97 by the sponsor due to strategic developments and adjustments. No patients were entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/135		<b>Status:</b> On-going	
<b>Title:</b> Linezolid (PNU-100766) in the Treatment of Gram Positive Bacteremia: An Open Label Phase II Study of Intravenous Therapy with Optional Oral Continuation					
<b>Start Date:</b> 08/15/97			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC William C. Williard, III, MC					
<b>Associate Investigators:</b>			MAJ Kenneth S. Azarow, MC		
Preston L. Carter, M.D.			COL William E. Eggebroten, MC		
MAJ Clifford A. Porter, MC			MAJ David M. Watts, MC		
MAJ Thomas K. Curry, MC			CPT Bret R. Hansen, MC		
<b>Key Words:</b> Bacteremia:gram positive, linezolid					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	9/30/97		

Study Objective: 1) To assess the efficacy and safety of intravenously and orally administered linezolid in the treatment of bacteremia; and 2) to assess pharmacokinetic parameters and their variance in this population, as well as the relationship between linezolid pharmacokinetics and therapeutic effects.

Technical Approach: This open label trial will test the efficacy and safety of Linezolid (PNU-100766) in at least 30 hospitalized adult patients with gram bacteremia. Those with negative cultures may remain in the study if they are clinically improving. Aztreonam may be administered to patients for gram negative organism coverage. At entry patient's APACHE II scores must be no higher than 23. Patients will receive linezolid 600 mg intravenously or orally twice a day. Duration of treatment will be 5 to 21 days. Patients must start study drug via the intravenous route of administration. They may switch to oral therapy after 3 days (4 doses) of IV therapy, but they must show clinical improvement (e.g., body temperature of <37.5 c, heart rate <100 BPM) for at least 24 hours before switching. Patients should have normal body temperature for 72 hours before cessation of study drug. The Short Term Follow-up will occur at 1 to 14 days post treatment, and the Long Term Follow-up will occur at 15 to 28 days post treatment.

Progress: Protocol is awaiting CIRO approval.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/122		<b>Status:</b> On-going	
<b>Title:</b> Linezolid in the Treatment of Skin/Soft Tissue Infections: An Open Label, Randomized, Dose Comparative Phase II Study of Low Dose Linezolid					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC William C. Williard, III, MC					
<b>Associate Investigators:</b>			MAJ Kenneth S. Azarow, MC		
Preston L. Carter, M.D.			COL William E. Eggebroten, MC		
MAJ Clifford A. Porter, MC			MAJ David M. Watts, MC		
MAJ Thomas K. Curry, MC			CPT Bret R. Hansen, MC		
<b>Key Words:</b> Infection:skin,soft tissue, Linezolid					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

**Study Objective:** 1) To assess the efficacy (clinical and microbiological) and safety of low dose linezolid in the treatment of skin/soft tissue infections; 2) to determine the minimum effective therapeutic dose of linezolid for skin/soft tissue infections. A success rate of  $\geq 75\%$  effective dose; and 3) to assess pharmacokinetic parameters and their variance, as well as the relationship between linezolid pharmacokinetics and therapeutic effects.

**Technical Approach:** This open label, randomized, dose comparative study will test the efficacy (clinical and microbiological) and safety of low dose linezolid, and will assess the minimum effective therapeutic dose of linezolid in adult patients with gram positive skin and soft tissue infections. For this study, low dose linezolid is defined as 600 mg/day (300 mg BID) or lower. Patients will be randomized to receive either 100 mg or 200 mg twice a day of linezolid. A third dosage group of 300 mg twice a day may be initiated during the course of the study. Depending upon the severity of the infection, patients may be hospitalized or may be treated entirely as outpatients. Patients may be treated entirely with oral linezolid. Hospitalized patients may be treated totally with intravenous linezolid, or intravenous linezolid followed by oral linezolid. Treatment duration will be 5 to 14 days (total IV plus oral treatment). Patients should be afebrile for 72 hours before cessation of study drug. Patients will have follow-up 1 to 14 days post treatment, and at 15 to 28 days post treatment. Safety labs will be drawn at end of treatment and at both follow-up visits. Pharmacokinetic blood samples will be drawn three times during the course of their participation.

**Progress:** Protocol was just approved, hence study has not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/032		<b>Status:</b> Completed	
<b>Title:</b> Phase III Population Pharmacokinetic Study for the Determination of Plasma Levels of Synercid (quinupristin/dalfopristin) in Treated Patients (Protocol JRV-135)					
<b>Start Date:</b> 11/17/95			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Surgery/General			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC William C. Williard, III, MC					
<b>Associate Investigators:</b>			LTC Patrick J. Offner, MC		
<b>Key Words:</b> Skin:infection, Synercids, plasma levels					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	10/20/95		

Study Objective: To evaluate Synercid plasma levels obtained in Phase III Synercid study patients in order to develop a population pharmacokinetic/pharmacodynamic model for the drug.

Technical Approach: This is an open-label, Phase III, randomized, comparative, multicenter study of Synercid versus standard therapy in the treatment of complicated gram-positive skin and skin structure infections. An adequate number of study sites will be initiated to enroll a sufficient number of patients for analysis (approximately 450-600 patients to obtain 300 evaluable, 150 per treatment arm). A pathogen isolation rate of at least 70% must be met to ensure that an adequate number of pathogens are identified. After giving informed consent and meeting the Inclusion/Exclusion criteria, patients will be randomly assigned to receive either Synercid iv 7.5 mg/kg every 12 hours, or standard therapy that is based on the clinical presentation of the patient and the susceptibility pattern of the causative pathogen: either Oxacillin iv 2g q 6h or Vancomycin iv 1g q 12h. Patients will be clinically assessed at baseline, on day 4, at the end of study treatment, and test of cure visit (14 to 28 days after treatment discontinuation).

Progress: Enrollment in this study was closed in Dec 96. No patients were entered at MAMC.



**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY,  
OPHTHALMOLOGY SERVICE**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/086		<b>Status:</b> On-going	
<b>Title:</b> A 6-Month, Randomized, Double-Masked Comparison of Fixed Combination of Latanoprost and Timolol with the Individual Components, Continuing into a 6-Month Open Label Safety Study of Fixed Combination...					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Kevin J. Chismire, MC					
<b>Associate Investigators:</b>					
LTC Vernon C. Parmley, MC			MAJ Roger K. George, MC		
MAJ William R. Raymond IV, MC			LTC Rob A. Mazzoli, MC		
MAJ Anthony R. Truxal, MC			MAJ Eugene F. May, MC		
CPT Keith F. Dahlhauser, MC			MAJ Thaddeus J. Krolicki, MC		
LTC Elizabeth A. Hansen, MC			COL Thomas H. Mader, MC		
<b>Key Words:</b> Glaucoma, Ocular hypertension, Combination, Latanoprost, Timolol, Individual Components					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To demonstrate that the fixed combination has a better IOP-reducing effect than the individual monotherapies. The differences from baseline diurnal IOP reduction after six months of treatment will be tested between the fixed combination and the monotherapy groups.

**Technical Approach:** This is a six month, randomized, double-masked, multicenter study with three parallel groups, continuing into a six month open label study with one treatment group. After a run-in period of two to four weeks on timolol 0.5% twice daily, the patients will be randomized at baseline into one of three treatment groups:

Group I - fixed combination of latanoprost 0.005% and timolol 0.5% in the morning and placebo in the evening.

Group II - Timolol 0.5% in the morning and evening.

Group III - Placebo in the morning and latanoprost 0.005% in the evening.

After six months of masked treatment, the patients will continue into a six month open treatment period when fixed combination is given in the morning to all patients. The patients shall be checked for eligibility within four weeks prior to baseline. A medical and ocular history as well as concomitant medications will be asked for and gonioscopy, perimetry, ophthalmoscopy, visual acuity and refraction, lid and slit lamp examination and IOP measurements will be performed. The masked treatment period comprises four visits at which visual acuity will be checked, lid and slit lamp examination performed, IOP measured, adverse events asked for and other ocular findings, as well as any changes in concomitant medications, will be recorded. Furthermore, at baseline, Week 26 and 52 heart rate and blood pressure measurements will be performed and the iris photographed. In addition, at Week 26 and 52 perimetry, refraction and ophthalmoscopy will be performed. During the open treatment period, patients will be examined at three visits. In addition, a follow-up contact will be performed two to four weeks after end of treatment

**Progress:** Currently screening for subjects, none have been entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/065		<b>Status:</b> On-going	
<b>Title:</b> A Parallel, Randomized, Double-Masked, Active Controlled, Multiclinic Study Comparing the Tolerability and Efficacy of 2.0% Dorzolamide Ophthalmic Solution and Orally Administered Acetazolamide in....					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Kevin J. Chismire, MC					
<b>Associate Investigators:</b>					
LTC Vernon C. Parmley, MC		MAJ Roger K. George, MC			
MAJ William R. Raymond IV, MC		LTC Rob A. Mazzoli, MC			
MAJ Anthony R. Truxal, MC		MAJ Eugene F. May, MC			
CPT Keith F. Dahlhauser, MC		MAJ Thaddeus J. Krolicki, MC			
LTC Elizabeth A. Hansen, MC		COL Thomas H. Mader, MC			
		MAJ Mary B. Grazko, MC			
<b>Key Words:</b> Ocular hypertension, glaucoma, dorzolamide, acetazolamide					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** Primary: To determine the incidence of systemic adverse events; including those most commonly reported with oral CAIs (e.g. headache, dizziness, nausea, paresthesia, fatigue as well as malaise, weight loss, depression, anorexia and loss of libido), in patients receiving 0.5% timolol maleate ophthalmic gel forming solution qd and acetazolamide 250 mg qid who are switched to 2.0% dorzolamide tid from acetazolamide compared to patients who remain on acetazolamide 250 mg qid. Secondary: In patients receiving 0.5% timolol maleate ophthalmic gel forming solution qd and acetazolamide 250 mg qid who are switched from acetazolamide to 2.0% dorzolamide tid compared to patients who remain on acetazolamide 250 mg qid: 1) To determine the incidence of systemic adverse experiences most commonly associated with oral CAI therapy (e.g. headache, dizziness, nausea, paresthesia, fatigue as well as malaise, eight loss, depression, anorexia and loss of libido. 2) To determine intraocular pressure.

**Technical Approach:** This is a parallel, randomized, double-masked, active-controlled study comparing the tolerability and efficacy of topical vs. oral carbonic anhydrase therapy added to 0.5% timolol maleate ophthalmic gel forming solution qd in patients with ocular hypertension or glaucoma. There is one open-label 3-week run-in period with Timoptic XE QD with acetazolamide 250 mg qid added on day -7. This is followed by a 12-week double-masked treatment period. The worse eye must be clinically suitable for additional IOP lowering on Day 1. Patients will be randomized at week 3 to one of 2 treatment groups. Intraocular pressure will be measured at 0900 (immediately pre-drop) and 1100 on Days 1, 15, 29, 57 and 85. Visual acuity, external ocular examination, slit lamp examination, funduscopy examination, visual field, and ocular symptoms will be evaluated on Days -21, -7, 1, 15, 29, 57 and 84. Safety laboratory tests will be done at baseline and on days 28 and 84.

**Progress:** Two subjects were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/060	<b>Status:</b> On-going
<b>Title:</b> Radial Keratotomy and Phototherapeutic Keratectomy: Comparison of Corneoscleral Integrity After Controlled Blunt Trauma to Post Mortem Eyes That Had Refractive Surgery		
<b>Start Date:</b> 03/21/97	<b>Est. Completion Date:</b> Jun 97	
<b>Department:</b> Surgery/Ophthalmology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Benjamin B. Chun, MC		
<b>Associate Investigators:</b> COL Thomas H. Mader, MC Rich L	CPT Mark L. Nelson, MC LTC Vernon C. Parmley, MC MAJ Lawrence J. White, MC	
<b>Key Words:</b> Keratotomy:radial, keratectomy:phototherapeutic, corneosclera, blunt trauma		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** The goal of this study is to examine and compare corneoscleral integrity, by means of controlled blunt trauma to the corneas of cadaver eyes obtained from the Lion's Human Eye Bank. The effects of phototherapeutic keratectomy (PTK) and radial keratotomy (RK) on postmortem corneas will be compared to controls.

**Technical Approach:** Three groups of eyes will be compared, two in each group. One group will have RK, done by an established Cornea Specialist, and the second group will have PTK, also done by an established Cornea Specialist who also specializes in the area of PTK. The third group will serve as control and will not have surgery. The intraocular pressure of each eye will be measured by Tonopen®. Intraocular BSS will be injected with a 27g needle until the IOP is 18.0mm Hg in each eye. Each eye will be placed in a container measuring 35mm X 45mm X 40mm, closely approximating the human orbit. 30 cc's of orbital volume not replaced by the eye will be filled with surgical lubricant and 4 X 4 gauze pads. The eye will be held in place by tight packing with gauze. The specimen will then be placed on the Instron where a blunt 1 cm diameter probe will descend toward the cornea at speed of 10cm/min. The computer will dynamically measure by way of graph, the breaking elongation, breaking load, yield point load, work of rupture and elastic stiffness of the globe. The data from all three groups will then be studied and compared. Total of 6 eyes will be utilized.

**Progress:** 14 eyes have been studied. Study has been hampered by difficulty in getting promised eyes.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/011		<b>Status:</b> Completed	
<b>Title:</b> Bovine Pericardium and Fascia Lata: Comparison in Physical Characteristics					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Benjamin B. Chun, MC					
<b>Associate Investigators:</b> LTC Rob A. Mazzoli, MC			CPT Mark L. Nelson, MC		
<b>Key Words:</b> Fascia lata, bovine pericardium, breaking load, breaking elongation, suture retention					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

**Study Objective:** The primary objective is to study and compare the physical characteristics of Fascia lata (FL), a material commonly used in Ophthalmology for ptosis repair, and Bovine Pericardium (BP), a newly available alternative.

**Technical Approach:** Two main groups of FL and BP will be analyzed: Breaking load and elongation test (42 samples FL and 42 samples BP) and Suture Retention test (24 samples FL and 24 samples BP). Each sample will have the dimensions 2 cm x 3 mm. The BP's are from Tissue-Guard, Bio-Vascular, inc., and the FL's are from the Fascia Lata Bank of the Wills Eye Hospital. Instron, a Servohydraulic Testing System, will be utilized as a materials tester, measuring Breaking Load, Breaking Elongation, and Suture Retention. After placing the sample in the hydraulics grip, the Instron will begin pulling apart the tissue at 10 cm/min, at the same time dynamically measuring the elongation, and at a certain point the breaking load, both by way of graph and raw data. Yield Point Load, Work of Rupture and Elastic Stiffness will be measured as a baseline strength test. Suture retention will be done similarly, with two 2mm bite with a 5-0 silk suture on each end of the FL and BP tissue. The sutures are then affixed to the hydraulics grip. The Instron will be gin separating at the same rate, measuring the amount of force until either the sutures pull through the tissue, breaks or the tissue tears completely. In applied use, the materials will be subject to mechanical loads far below those applied during testing. Out goal is to demonstrate that BP is not more than 20% weaker than FL at a magnitude level at .05 with 80% probability. This level of strength reduction should be more than adequate to accommodate any stresses applied in a physiological situation. Independent t-test will be used to compare the groups.

**Progress:** Results indicate that maximal load and suture retention of bovine pericardium and fascia lata are comparable. However, the cross sectional breaking load of the bovine pericardium, appears to be nearly twice that of the fascial lata. Possible ophthalmic roles include lid spacer grafts, tarsal substitutes, frontalis suspension, orbital implant and glaucoma seton coverage, as well as other applications where fascia lata or banked sclera is used.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/140		<b>Status:</b> Completed	
<b>Title:</b> A Parallel, Randomized, Double-Masked, Multicenter Study Comparing the Effect of Dorzolamide 2% to Pilocarpine 2% as Adjunctive Therapy to Timolol Maleate Ophthalmic Gel Forming Solution 0.5% in ....					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Roger K. George, MC					
<b>Associate Investigators:</b>			COL Kevin J. Chismire, MC		
<b>Key Words:</b> Intraocular pressure, Dorzolamide, Pilocarpine, Timolol Maleate					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** Primary: To assess the effectiveness of dorzolamide 2% tid added to timolol maleate ophthalmic gel forming solution 0.5% qd compared with pilocarpine 2% qid added to timolol maleate ophthalmic gel forming solution 0.5% qd at morning trough (hour 0). Secondary: To assess the effectiveness of dorzolamide 2% added to timolol maleate ophthalmic gel forming solution 0.5% qd compared with pilocarpine 2% qid added to timolol maleate ophthalmic gel forming solution 0.5% qd at morning peak (hour 2). To collect safety data on dorzolamide 2% given concomitantly with timolol maleate ophthalmic gel forming solution 0.5% qd. To collect safety data on pilocarpine 2% given concomitantly with timolol maleate ophthalmic gel forming solution 0.5%.

**Technical Approach:** This is a parallel, randomized, double-masked active-controlled study. There is one open-label 3-week run-in period followed by a 12-week double-masked treatment period. The worse eye must be clinically suitable for additional IOP lowering on Day 1. Patient will be randomized at week 3 to one of 2 treatment groups. Intraocular pressure will be measured at 0900 (immediately pre-drop) and 1100 on days 1, 15, 29, 57, and 85. Visual acuity, external ocular examination, slit lamp examination, funduscopy examination, visual field, and ocular symptoms will be evaluated on Days -21, 1, 15, 29, 57 and 85. Between group comparisons with regard to percent change in IOP from baseline will be made using analysis of variance techniques. The incidence rates for adverse experiences and ocular sign will be compared using Fisher exact-test.

**Progress:** The study was closed by the sponsor Jan 97 due to sufficient patient accrual. Twelve patients were enrolled in the study; eight patients were randomized to the study drug.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/061		<b>Status:</b> Terminated	
<b>Title:</b> The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Thomas H. Mader, MC					
<b>Associate Investigators:</b> LTC Vernon C. Parmley, MC Troy H. Patience, B.S. MAJ J. Wayne Riggins, MC			MAJ Steven C. Hadley, MC Gilbert G R. Doyle Stulting, M.D., Ph.D.		
<b>Key Words:</b> Myopia, photorefractive keratectomy, military personnel					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The purpose of the study is to determine if excimer laser photorefractive keratectomy (PRK) is a suitable procedure for use in active duty army personnel for the correction of myopia.

**Technical Approach:** Approximately fifty personnel in U.S. Army Special Operations, between the ages of 21-50, who meet the inclusion / exclusion criteria will be subjects for the study. Inclusion criteria include cycloplegic refraction between -1.50 and -4.50 diopters, best corrected visual acuity of 20/40 or better in both eyes, and 1 diopter or less of central astigmatism as measured by keratometer. The exclusion criteria include a history of eye surgery or eye infection, corneal neovascularization > 1mm from the corneal/sceral junction, immunocompromised state or systemic corticosteroid medications. Following appropriate preoperative workup, the non-dominant eye of each subject will undergo excimer laser photorefractive keratectomy. Four to six months later, PRK will be performed on the second eye when 20/20 best corrected visual acuity with less than +1 haze has been achieved. Following this procedure, subjects will be followed at specified intervals to monitor the success of the procedure. Subjects will be tested with night vision goggles as well as sighting devices to include those on open rifle sights, rifle scopes, laser range finding devices and target acquisition devices. We will obtain keratometry and cycloplegic refraction on individuals both at sea level and at altitudes in excess of 10,000 feet.

**Progress:** No patients were entered because the subject population were either on field duty or deployed too often to be able to conduct the study; therefore, it was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/119		<b>Status:</b> On-going
<b>Title:</b> The Use of Photorefractive Keratectomy on Active Duty U.S. Army Personnel for the Correction of Myopia				
<b>Start Date:</b> 07/18/97		<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> Surgery/Ophthalmology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Thomas H. Mader, MC				
<b>Associate Investigators:</b>		LTC Vernon C. Parmley, MC		
<b>Key Words:</b> Photorefractive keratectomy, Escimer, Radial Keratotomy, Myopia				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** To determine if excimer laser photorefractive keratectomy (PRK) is a suitable procedure for use on active duty Army personnel for the correction of myopia.

**Technical Approach:** Refractive surgery of myopia with the excimer laser is of current command interest because of its potential to be performance enhancing in myopic active duty soldiers. Many active duty soldiers have an interest in this surgery and may elect to have it performed by civilian ophthalmologists at their own expense. There has been no prospective Army study to evaluate the effect of myopic excimer laser refractive surgery on active duty soldiers and how it affects the soldier's ability to perform his duties. This study proposes to 1) recruit a cohort of myopic active duty soldiers who voluntarily agree to participate, 2) prior to any treatment, evaluate their vision and its impact on certain basic military performance standards (such as qualifying with an M-16 rifle), 3) treat the myopia in both eyes by surface ablation of the cornea with an excimer laser, and finally 4) follow and re-evaluate vision and performance standards on these individuals for at least two years after treatment to examine the effect of the surgery on performance. One of the purposes of this study is to evaluate the potential of using this procedure to treat myopic soldiers thereby improving their ability to function in a combat environment and improve mission efficacy.

**Progress:** This protocol has received approval from CIRO and has been forwarded to MRMC for funding.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/153		<b>Status:</b> On-going	
<b>Title:</b> Refractive Changes at High Altitude More Than Four Years Following Radial Keratotomy					
<b>Start Date:</b> 09/20/96			<b>Est. Completion Date:</b> Nov 96		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Thomas H. Mader, MC					
<b>Associate Investigators:</b> Robert Gibson, O.D.			MAJ Lawrence J. White, MC		
<b>Key Words:</b> Radial keratotomy;refractive changes, high altitude					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>9/30/97</b>

**Study Objective:** Our objective is to observe changes in corneal shape and visual acuity that may take place in subjects four years or more following radial keratotomy when these individuals are exposed to two weeks at high altitude.

**Technical Approach:** Our research will be conducted as part of an American medical research project in Nepal in October of 1996. Our subjects will come from members of this research group who will be hiking along a predetermined path of increasing altitude. We will select two study groups for our experiment. The first group will consist of four volunteers who have had radial keratotomies at least four years prior to this study. We will record and examine several ocular parameters on these individuals, both at sea level and following 48 hour exposure to 9,100, 11,350, 14,000 and 15,600 feet. Repeat sea level measurements will be made one week after return to the U.S. These parameters include visual acuity, near point of accommodation, cycloplegic refraction, intraocular pressure, corneal keratometry, and central corneal thickness. Oxygen saturation will also be monitored and recorded using a pulse oximeter. The second study group will consist of 4 normal myopes (nearsighted persons). In these individuals, we will also measure the above listed parameters at the same altitudes as listed above. We will then compare data to see if a significant difference exists between the two groups.

**Progress:** Four subjects were studied in this first long term study of exposure to altitude after radial keratotomy. There were more variables than expected and one person developed more far sightedness than was expected.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/125	<b>Status:</b> Completed
<b>Title:</b> Efficacy of Detection of Intraocular and Intraorbital Plastic Foreign Bodies by Magnetic Resonance (MR) and Computed Tomography (CT) Imaging in the Goat		
<b>Start Date:</b> 06/10/94	<b>Est. Completion Date:</b> Apr 95	
<b>Department:</b> Surgery/Ophthalmology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Rob A. Mazzoli, MC		
<b>Associate Investigators:</b>		
COL Thomas H. Mader, MC	CPT Lilia A. Fannin, MC	
COL David P. George, MC	LTC Vernon C. Parmley, MC	
LTC Miquel J. Rovira, MC	MAJ Vincent B. Ho, MC	
	LTC William F. Coughlin III, MC	
<b>Key Words:</b> Foreign bodies:intraocular, Foreign bodies:intraorbital, Foreign bodies:plastic, MRI, CT scan,Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/08/96

**Study Objective:** 1. To determine the efficacy of CT and MR imaging in detecting intraocular or intraorbital plastic foreign bodies in the goat. 2. To determine if intravenous contrast during CT and MR imaging improves the detection of intraocular or intraorbital plastic foreign bodies.

**Technical Approach:** Twelve goats will be used to evaluate the efficacy of CT and MR imaging in detecting plastic foreign bodies in the eye and around the eye. The goats will be sedated, anesthetized, and intubated prior to the surgical placement of 1 to 6 plastic foreign bodies (sizes ranging from 1/32 - 1/4 inch) in the eye. The wound will not be closed so as to simulate an eye injury. Plain film x-ray, CT and MR images will be obtained. Intravenous dye will be given for the imaging studies. The fellow eye will be the control. After the CT and MR studies are completed, the goats will be sacrificed. Plain films, CT and MR images will be evaluated by four masked physicians (two radiologist and two ophthalmologists). These doctors will not know which eye has the plastic foreign bodies. From these evaluations, we will determine if CT or MR are equally effective in detecting the foreign bodies and we will determine if the intravenous dye improved the detection of the plastic foreign bodies.

**Progress:** Twelve goats were studied. Neither CT nor MR are sufficiently sensitive to detect intraocular or intraorbital foreign bodies from plastic land-mines.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/121		<b>Status:</b> On-going	
<b>Title:</b> Refractive Changes During Exposure to the Hyperbaric Environment Following Radial Keratotomy Surgery					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Mark L. Nelson, MC					
<b>Associate Investigators:</b> Chun GG LTC Vernon C. Parmley, MC			Edson T COL Thomas H. Mader, MC		
<b>Key Words:</b> Radial keratotomy, hyperbaric environment, corneal shape, visual acuity, refraction, intraocular pressure					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** Our objective is to verify significant changes in corneal shape, visual acuity, refraction and intraocular pressure that may take place in subjects within two years following radial keratotomy when these individuals are exposed to the hyperbaric environment.

**Technical Approach:** We will select three groups for our experiment. The first study group will consist of 13 U.S. Navy volunteers who have had bilateral radial keratotomies within two years prior to this study. (Currently RK's are disqualifying for flight status and entry into the military, but not disqualifying for retention in the military.) We will record and examine several ocular parameters, at sea level and immediately after exposure to depth equivalent to 50 feet of sea water: 1) cycloplegic refraction, 2) intraocular pressure, 3) corneal keratometry, and 4) central corneal thickness. Barometric pressure will also be recorded. Duration will be the maximum allowed at that depth for a no decompression dive (100 minutes). This depth was chosen because military divers carry out most of their missions at or above this depth, and this is an average depth for recreational diving. The second study group will also consist of 13 U.S. Navy volunteers who have had bilateral radial keratotomies within 2 years prior to the study. This group will be treated exactly the same as the first group except they will wear goggles with 100% oxygen infused into them at depth. The third study group will consist of 13 active duty volunteers with no previous ocular surgery. In these individuals, we will measure the above listed parameters at sea level and immediately after hyperbarics at 50 fsw. We will then compare data to see if a significant difference exists between the three groups. A power analysis was performed, assuming a 0.25 diopter intraobserver variability and a significant myopic shift of 0.50 diopters. The required sample size computed was 25 eyes. We will have 26 eyes in each study group.

**Progress:** Study has not yet started pending final approval of consent form by DCI.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/105	<b>Status:</b> Completed
<b>Title:</b> Ocular Findings in Robinow (Fetal Face) Syndrome		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Apr 97	
<b>Department:</b> Surgery/Ophthalmology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Mark L. Nelson, MC		
<b>Associate Investigators:</b>		
CPT Keith J. Wroblewski, MC	MAJ William R. Raymond IV, MC	
LTC Elizabeth A. Hansen, MC	CPT Benjamin B. Chun, MC	
Mark J. Stephan, M.D.	LTC Rob A. Mazzoli, MC	
<b>Key Words:</b> Robinow syndrome, lamellar cataracts		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To report an ocular finding in three patients with Robinow syndrome that has not been previously reported in the literature. Robinow syndrome consists of characteristic facies, mesomelic brachymelia of the arms, hypoplastic genitalia, and short fingers. Previously reported ophthalmic findings include hypertelorism, wide palpebral fissures, and lacrimal abnormalities.

**Technical Approach:** Both an autosomal dominant and autosomal recessive form of Robinow syndrome are described in the literature, with the recessive form generally being more severe. This series of three patients has an autosomal dominant pattern of inheritance of both the previously reported characteristics of Robinow syndrome, as well as the lamellar cataracts. This type of cataract may be difficult to see in infancy and early childhood during a routine physical examination by a pediatrician. If missed on examination, this could result in deprivation amblyopia and permanent visual loss. Pediatricians and ophthalmologists need to be aware that lamellar cataracts are potentially a possible finding in the Robinow syndrome, and these patients should receive a detailed eye exam.

**Progress:** Three patients were studied. It was found that all three patients had lamellar cataracts and that this had not been previously reported in association with Robinow syndrome.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/029		<b>Status:</b> Terminated	
<b>Title:</b> A Prospective, Randomized Clinical Trial Comparing Topical Prednisolone 1% to Diclofenac 0.1% in the Treatment of Pseudophakic Cystoid Macular Edema (PCME)					
<b>Start Date:</b> 11/17/95			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark F. Torres, MC					
<b>Associate Investigators:</b>			MAJ Thaddeus J. Krolicki, MC		
<b>Key Words:</b> Macular edema, prednisolone, diclofenac					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					9/30/97

**Study Objective:** (1) To objectively assess the efficacy of topical diclofenac as a treatment modality (monotherapy) for PCME. (2) To compare prednisolone and diclofenac as treatment for PCME. (3) To assess the safety of long term (potentially up to four months) use of topical diclofenac.

**Technical Approach:** Patients who are between 6 - 52 weeks post cataract surgery where found to have PCME will be referred to a vitreoretinal specialist who will confirm the PCME via a contact lens biomicroscopic examination and serve as a "blind" observer for subsequent follow-up evaluations for that particular patient. If a patient elects to enroll into the study, they will be required to return within 72 hours to have an undilated, best-corrected visual acuity examination using a standardized eye chart from the Early Treatment in Diabetic Retinopathy Study (ETDRS). The patient will be randomized to receive either prednisolone 1% or diclofenac. The investigator/examiner will be blind with respect to which drug each patient is using, making the study a single blind, open label, prospective, randomized clinical trial (multi-center). Follow-up examinations will be performed at 4, 8, 12, and 16 weeks following initiation of drug therapy. At each follow-up, an investigator other than the masked retina specialist will perform the initial portion of the examination, to include completion of the questionnaire and ETDRS visual acuity. During the interval visits the patients will be given a questionnaire asking for subjective rating on their symptoms and any side effects noted when using the drug. The patient will then be examined by the blind retina specialist who will perform an angiogram and grade the PCME as either "present" or "absent". If present, it will be scored as "improve," "unchanged," or "worse." At 8, 12, and 16 weeks, the same evaluation sequence as described at 4 weeks will take place. All angiograms will be reviewed in a masked fashion and independent grades will be compared to those from the original examiner to ensure inter-examiner consistency. The study endpoint will be at the four month follow-up interval. If PCME is still present, it will be left to the investigators to determine any additional therapy. The codes will be broken and the provider will be informed as to which drug was used. In any case, if the patient is willing, investigational follow-up would continue at one month intervals to maximize data received for subgroup analysis.

**Progress:** Three subjects were entered at MAMC. The project was terminated due to an insufficient number of subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/081		<b>Status:</b> Completed	
<b>Title:</b> The Contribution of the Donor Cornea to Final Corneal Curvature in Penetrating Keratoplasty					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark F. Torres, MC					
<b>Associate Investigators:</b> LTC Vernon C. Parmley, MC			COL Thomas H. Mader, MC CPT Keith J. Wroblewski, MC		
<b>Key Words:</b> Keratoplasty, corneal curvature, donor cornea					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					9/30/97

Study Objective: To determine the potential contribution, if any, of the donor corneal tissue to final corneal curvature and refractive status following corneal transplantation.

Technical Approach: We will identify pairs of corneal transplant recipients who received their donor corneal tissue from the same donor. Corneal curvature measurements will be determined for this study group, and then compared against similar measurements from a control group consisting of randomly identified and paired corneal transplant recipients. Data analysis will consist of comparison of the means from each group.

Progress: Thirty four patients were entered.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/017	<b>Status:</b> Completed
<b>Title:</b> Pseudotumor Cerebri Associated with Minocycline Therapy		
<b>Start Date:</b> 11/15/96	<b>Est. Completion Date:</b> Dec 96	
<b>Department:</b> Surgery/Ophthalmology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark F. Torres, MC		
<b>Associate Investigators:</b> MAJ Eugene F. May, MC		
<b>Key Words:</b> Pseudotumor Cerebri, minocycline, acne		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To determine the occurrence of both symptomatic and asymptomatic Pseudotumor Cerebri among patients receiving oral Minocycline for the treatment of Acne.

**Technical Approach:** The failure to diagnose Pseudotumor Cerebri may be due to the lack of symptoms, or the lack of recognition of a potential association with Minocycline therapy. Since Minocycline is a common and popular treatment of Acne, this study will determine the incidence of Psuedotumor Cerebri in a sample population of patients receiving Minocycline therapy for the treatment of Acne.

**Progress:** Three patients were studied who presented with symptoms of headache and transient visual obscurations and who had papilledema on eye exam consistent with a diagnosis of intracranial hypertension. Thirteen patients were evaluated, 4 males and 9 females. Three females complained of headaches while taking minocycline and one female complained of transient visual obscurations. Five of the 9 females were considered to be overweight by BMI, and two of those were obese. Three of the 4 males were overweight by BMI. None of the 13 patients had papilledema. The investigators concluded that minocycline use has been associated with the development of intracranial hypertension. However, this study demonstrates that the prevalence of this complication is low in a series of patients not seeking medical treatment for headaches or visual symptoms.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/135		<b>Status:</b> Completed	
<b>Title:</b> Anterior Capsular Contraction in Phacoemulsification					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith J. Wroblewski, MC					
<b>Associate Investigators:</b> LTC Vernon C. Parmley, MC			CPT Keith F. Dahlhauser, MC COL Thomas H. Mader, MC		
<b>Key Words:</b> Cataract, capsular contraction syndrome, phacoemulsificatioin					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine risk factors for capsular contraction syndrome after phacoemulsification and posterior chamber intraocular lens placement. We will determine the incidence of capsular contraction syndrome between three different intraocular lenses: silicone, acrylic and polymethylmethacrylate performed by one surgeon.

**Technical Approach:** Our study will retrospectively examine every cataract extraction here at Madigan utilizing three different types of intraocular lenses. We will examine the risk factors for contraction of the anterior lens capsule and study the incidence of lens decentration of the intraocular lens implant. Specifically, is there a relationship between the type and composition of the lens and the incidence of decentration? Is there a relationship between preoperative uveitis, post-operative anterior chamber inflammation and capsular contraction syndrome? We will use chi-square analysis to examine the incidence of contraction syndrome with the type of lens used, capsule contraction with the size of the operative capsulorhexis, and the preoperative history of uveitis with contraction. A logistic regression creating a formula for the different variables could be created and could help determine the risk factors for the different variables.

**Progress:** Forty-five phacoemulsification procedures with foldable silicone intraocular lens implantations were studied. Nine patients had radial anterior capsulotomy with four relaxing radial incisions. Three of the nine patients complained of decreased visual acuity and glare noted between days 30 and 54, post-operatively. Mean visual acuity of these symptomatic patients was 20/50. Two other patients had chronic anterior chamber inflammation but no symptoms. Inflammation resolved abruptly after YAG capsulotomy. Decentration was observed in three patients which resolved after capsulotomy. It is concluded that postoperative inflammation may improve after YAG capsulotomy. YAG capsulotomy stabilizes decentration. Early anterior capsule monitoring with appropriate early anterior capsulotomy may prevent serious complications.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/154		<b>Status:</b> Completed	
<b>Title:</b> Pulfrich's Phenomenon in Patients with Optic Neuropathy					
<b>Start Date:</b> 09/20/96			<b>Est. Completion Date:</b> Dec 96		
<b>Department:</b> Surgery/Ophthalmology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith J. Wroblewski, MC					
<b>Associate Investigators:</b> Brazelo MB			MAJ Eugene F. May, MC Troy H. Patience, B.S.		
<b>Key Words:</b> Pulfrich'sphenomenon, optic neuropathy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** To study the prevalence of Pulfrich's phenomenon in patients with optic neuropathy and see how it correlates to pupillary function, visual field defects, contrast sensitivity and binocular vision.

**Technical Approach:** Fifty Ophthalmology Clinic patients with a history of optic neuropathy, as evidenced by clinical history and examination, will be recruited for this study. On the same day of each week for three months, we will perform tests on each subject for visual acuity, Humphries Automated Visual Fields, contrast sensitivity, Randot Viewer Stereoacuity, and Pulfrich phenomenon. In addition, one of the associate investigators will perform the swinging flashlight-test in order to grade a relative afferent pupillary defect using neutral density filters. The first portion of data analysis will be determining whether a subject's description of his/her visual experience during testing for Pulfrich's correlates with the laterality of the optic neuropathy. Secondly, correlation analysis will be performed between the density (in log units) of neutral density filter necessary to neutralize each subjects Pulfrich's phenomenon with four other visual parameters. The presence of any correlation between the "amplitude" of Pulfrich's phenomenon and any of the other parameters would support the hypothesis that the presence and extent of Pulfrich's phenomenon in a patient is an objective and quantitative measure of optic nerve dysfunction.

**Progress:** Twenty-seven patients were entered. Pulfrich's phenomenon is not a specific indicator of the side or the severity of an optic neuropathy except when there is a high grade afferent pupillary defect. The stereoillusion does not correlate well with visual field changes, contrast sensitivity, or stereoacuity.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY  
ORTHOPEDIC SURGERY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/052		<b>Status:</b> Completed
<b>Title:</b> Does Insertion of a Cortical Bone Screw Into Bone Change the Torsional Strength? A Biomechanical Study				
<b>Start Date:</b> 02/21/97		<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> Surgery/Orthopedic		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT George K. Bal, MC				
<b>Associate Investigators:</b>		Henley MB		
<b>Key Words:</b> Bone:torsional strength, bone screw				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

**Study Objective:** To evaluate the effect of a single insertion and removal of an orthopedic bone screw on the torsional strength of the screw.

**Technical Approach:** We will test cortical bone screws of 2.7, 3.5 and 4.5 mm sizes. We will also test cannulated screws of 3.5, 5.0, 6.5, and 7.3 mm sizes in stainless steel and titanium. The screws will be divided into 4 groups consisting of ten screws. Group 1 will be a control group, these screws will not be inserted. Groups 2, 3, and 4 will be inserted into drilled, tapped holes in cadaveric fresh frozen human femora. Group 2 will be inserted directly into bone, Group 3 through a plate into a centered hole, and Group 4 through a plate into an eccentric hole. The screws will be inserted with a digital torque wrench to a pre-determined force. The screws will then be removed and tested to torsional failure, along with the control groups, on a material testing machine.

We will analyze the torsional failures of the various screw groups and compare this to the controls. The applied torque will be sampled at 25 Hz, and recorded on a personal computer using data acquisition software (LabVIEW, National Instruments, Austin, TX 78730). The torsional loads will be plotted versus time. One second of data collected immediately before the failure point will be averaged to obtain the failure torque for each screw. An analysis of variance will be performed (StatView, Abacus Concepts, Berkeley, CA 94704) on the failure torque data to determine the effect of the various treatments. Post hoc testing will be performed using Fisher's PLSD multiple comparison test with  $p < 0.05$  to determine significance.

**Progress:** 120 screws were evaluated. The current practice of discarding bone screws after a single insertion and immediate removal is based on the manufacturer's refusal to guarantee screw integrity. Study results show no change in screw strength. Disposing of expensive cortical bone screws after a single insertion may be unnecessary.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/051		<b>Status:</b> On-going
<b>Title:</b> Comparison of Small Bone Cannulated Screw Systems				
<b>Start Date:</b> 02/21/97		<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Surgery/Orthopedic		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT George K. Bal, MC				
<b>Associate Investigators:</b>		LTC D. E. Casey Jones, MC		
<b>Key Words:</b> Bone:screw systems, compression, pull-out strength				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** To compare compression and pull-out strengths of three different small bone cannulated screw systems - the Accumed 'Accutrak' screw, the Herbert-Whipple screw, and the Synthes 3.0mm cannulated screw.

**Technical Approach:** We will evaluate four different cannulated screws: an ASIF 3.5mm cannulated screw, Synthes 3.0mm cannulated screw/washer, Accumed's Accutrak screw, and Zimmer's Herbert-Whipple screw. The screws will be divided into three study groups designed to measure compression, pull-out strength, and compression holding. There will be ten screw of each type in each study group. We will use a synthetic cancellous bone material of uniform density, and a washer shaped strain gauge for collecting data. A servohydraulic testing machine will be used for measuring pull-out strength. The data will be evaluated by random-effects analysis of variance.

**Progress:** Have evaluated laboratory instruments for study and performed pilot tests. Currently awaiting testing materials to begin actual study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/094		<b>Status:</b> On-going	
<b>Title:</b> Autologous Cartilage Grafting for Talar Dome OCT Lesions					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Jun 01		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT George K. Bal, MC					
<b>Associate Investigators:</b> R.V. Williamson			MAJ Patrick St Pierre, MC		
<b>Key Words:</b> Osteochondral defects, lesions, autologous cartilage grafting					
<b>Accumulative</b> <b>MEDCASE Cost:</b>		\$0	<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b> 9/30/97
			\$0.00		

**Study Objective:** To evaluate the functional outcomes of the treatment of talar OCD lesions in a randomized, prospective trial.

**Technical Approach:** Will prospectively evaluate two methods of treating talar OCD lesions. Subjects will be randomized to two Groups; arthroscopic debridement and drilling of the OCD lesion, or open debridement with cartilage grafting. We will use arthroscopic harvesting techniques from the ipsilateral knee- as is currently used for OCD lesions of the knee. The post-operative rehabilitation protocols will be the same for both Groups. Subjects will have scheduled follow-up at 2 weeks, 6 weeks, 3 months, 6 months, 1 year, and 2 years. A standard outcome analysis questionnaire will be used at the 6 month, 1 year, and 2 year follow-ups.

**Progress:** Awaiting identification of appropriate subjects for enrollment into the study protocol.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/107		<b>Status:</b> On-going	
<b>Title:</b> Evaluation of Lateral Ankle Stress Testing With and Without Anesthesia					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Jan 98		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT George K. Bal, MC					
<b>Associate Investigators:</b>			MAJ Kirk Willard, MC		
<b>Key Words:</b> Ankle, stress testing, anesthesia					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97	

Study Objective: To determine the significance of pain response/inhibition that occurs during lateral ankle stress testing.

Technical Approach: We will evaluate ankle stress radiographs (using the TELOS Device) without anesthesia, with local anesthetic, and finally with regional/general anesthesia. The sample population will be patients with chronic ankle pain and/or instability seen at Madigan Orthopedic/Podiatry Clinic. Between 50-100 subjects will be studied. The subject will have ankle stress radiographs performed, then repeated with a local anesthetic (intra-articular vs peroneal nerve block). If determined that the patient requires surgery, intra-operative stress radiographs will be performed after induction of regional/general anesthesia. Approximately 20 control subjects will be selected from orthopedic patients requiring surgery. They will have preoperative ankle stress radiographs done, and again after induction of anesthesia for their scheduled surgery. No local anesthetic injections will be used for control subjects. The data collected will be measurements of tibio-talar angle and anterior subluxation from the stress radiographs. These will be evaluated using an independent t-test, and repeated measures analysis.

Progress: 6 subjects were entered in FY 97, for a total of 10 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/108		<b>Status:</b> On-going
<b>Title:</b> Subtalar Joint Stress Radiography				
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Jun 97	
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT George K. Bal, MC				
<b>Associate Investigators:</b>			MAJ Kirk Willard, MC	
<b>Key Words:</b> Subtalar joint, stress, radiography				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: To establish the normal variation of the subtalar joint stress angle. We will also attempt to standardize the method of measurement.

Technical Approach: The normal values of talo-calcaneal angle will be looked at using the TELOS Device and stress radiographs. The sample population will come from patients seen at the Madigan Orthopedic/Podiatry Clinic. We will utilize up to 200 normal subjects with no prior history of ankle injuries. The subjects will have an ankle stress radiograph performed using the TELOS device. After the radiograph is complete, no further participation in the study will be needed. The talo-calcaneal angle will be measured off of the stress radiograph. This data will be evaluated for potential co-variants, and a normal range will be determined with confidence intervals.

Progress: 15 subjects were entered in FY 97, for a total of 17 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/095		<b>Status:</b> On-going
<b>Title:</b> Delayed versus Immediate Open Repair of Achilles Tendon Rupture; A Randomized Prospective Trial				
<b>Start Date:</b> 05/16/97		<b>Est. Completion Date:</b> Jun 01		
<b>Department:</b> Surgery/Orthopedic		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT George K. Bal, MC				
<b>Associate Investigators:</b> LTC John D. Pitcher Jr., MC		R.V. Williamson		
<b>Key Words:</b> Achilles tendon, delayed versus immediate repair				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		9/30/97

Study Objective: To evaluate the differences in surgically repairing Achilles tendon ruptures immediately, or waiting 10-14 days to perform the repair.

Technical Approach: All patients identified with acute Achilles tendon ruptures, who are being considered for surgical repair, will be presented the option of enrolling in this study. The subjects will be randomized to one of two Groups: Group I - Immediate surgical repair (within 72 hours) of the Achilles tendon, or Group II - delayed (between 10 and 14 days) surgical repair of the tendon rupture. The patients will be randomized using a computer generated randomization table. We will initially randomize the first ten patients, and a subsequent power analysis will be performed at 6 month follow-up to insure that enough patients are enrolled to make our results significant. The next 20 patients will be randomized using a second computer generated table. The post-operative course for both Groups will be the same. The patients will be followed up at 2 week, 6 week, 9 week, 6 month, 12 month, and 24 month intervals. They will be evaluated for post-operative complications and functional outcome.

Progress: 2 subjects were entered in FY 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/098	<b>Status:</b> On-going
<b>Title:</b> Fixation of Salter Osteotomies with Bioabsorbable Pins		
<b>Start Date:</b> 04/25/97	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery/Orthopedic	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Christopher P. Cannon, MC		
<b>Associate Investigators:</b>		
MAJ Ronald E. Nielsen, VC	Song KM	
Welch R	A. Tencer	
	MAJ Clyde T. Carpenter, MC	
<b>Key Words:</b> Osteotomy, bioabsorbable pins, pelvis, goats, children, Animal Study		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	9/30/97

**Study Objective:** To review the feasibility of using bioabsorbable pins when doing pelvic osteotomies in children. We will do osteotomies on the pelvis of goats which are similar in size to a toddler.

**Technical Approach:** The first phase will involve an animal study. We have determined that the pelvis of a goat is near the size and orientation of a child's pelvis who might undergo a Salter pelvic osteotomy. We will perform a unilateral pelvic osteotomy, place bone graft, and insert pins to hold the pelvic osteotomy. The bone graft will be harvested from the ipsilateral iliac crest. The goat will be given antibiotics perioperatively. The second phase (which will involve another protocol and will be based on the goat studies) will be a multicenter prospective clinical trial of children undergoing Salter osteotomies for hip dysplasia. We will randomize the children on the basis of their institution so that all children treated at a given institution would be treated in a similar manner. Selection criteria would be children less than 3 years of age, neurologically and mentally normal, and requiring a Salter osteotomy for the treatment of congenital dislocation of the hip. We will seek to enroll 50 children (25 treated with Steinman pins and 25 children treated with bioabsorbable pins) in each group. We would endeavor to enroll 3 centers for each group for a total of 6 centers involved with each center treating approximately 8 children. We would use a fairly large human study because of the need for large enough numbers to address statistically the outcome.

**Progress:** Has not started awaiting CRDA approval.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/110	<b>Status:</b> Completed
<b>Title:</b> A Multicenter Study of Treatment of Growth Arrest by Excision of Physeal Bars		
<b>Start Date:</b> 04/21/95	<b>Est. Completion Date:</b> Dec 95	
<b>Department:</b> Surgery/Orthopedic	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Clyde T. Carpenter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Growth, physeal bars, excision		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To perform a multi-center, retrospective collection of data on the treatment of deformities arising from growth arrest by the excision of physeal bars bones.

**Technical Approach:** This preliminary retrospective study will include all patients having had a physeal bar excision and a minimum of two years follow-up. Information collected will include: (1) age, sex, race and body habitus of the patients; (2) etiology, bone involved, placement, age, and size of the bar; and (3) the degree of angular deformity and limb length discrepancy existing prior to excision of the bar. Separate forms will be used to document the specifics of surgical intervention, any subsequent interventions, and to determine results at the end of the follow-up period. Each patient will be analyzed in terms of his/her outcome. The information collected will be used to determine the methods of treatment most often yielding acceptable results in specific situations. Student's t-test, chi-square evaluation of four fold tables, regression analysis or other statistical methods will be utilized as appropriate depending on the nature of the retrospectively collected data.

**Progress:** One hundred patients were entered at the Shriner's hospital. MAMC participation is complete. Data analysis is to be done elsewhere.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/176		<b>Status:</b> On-going	
<b>Title:</b> Computer Assisted Measurement of Scoliosis from Digitized Radiographs versus Traditional Cobb Angle Measurement					
<b>Start Date:</b> 12/17/93			<b>Est. Completion Date:</b> Sep 93		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Clyde T. Carpenter, MC					
<b>Associate Investigators:</b> MAJ Donald V. Smith, MC			LTC Richard W. Kruse, MC MAJ John W. Dietz, MC		
<b>Key Words:</b> scoliosis, computer assisted meaurements					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$500.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The purpose of this study is to determine the interobserver and intraobserver error and accuracy of measurement in determining Cobb angle measurements of scoliosis and kyphosis using the digitized radiographs and measuring techniques available in the Medical Diagnostic Imaging System (MDIS).

**Technical Approach:** In the first phase fifty anterior-posterior or posterior-anterior spine radiographs will be collected in the Orthopaedic Clinic by two of the Investigators. These radiographs must demonstrate coronal plane deformity of 10 degrees or more. During this the radiographs will be modified to obscure the patients' names and copy the radiographs into the MDIS system. Each radiograph MDIS image will be assigned a random number. The MDIS image and its corresponding radiograph will have different numbers and a log will be created showing which random numbers have been assigned to corresponding images. The examiners will be blinded to this information.

The images will be measured in random order. All measurements will be made using the Cobb method. A line will be drawn along the superior end plate of the upper vertebra to the inferior end plate of the lower vertebra. Some radiographs will have 2 measurable curves. Only one curve from the thoracic and one from the lumbar area will be measured. Measurements on radiographs will be done with pencil and protractors usually employed in the Orthopaedic Clinic. Measurements on MDIS images will be done by choosing lines along end plates with the mouse and indicator. Actual measurements will be made by each of four observers. Measurements will be recorded on a data sheet.

**Progress:** 50 scoliosis radiographs were selected and prepared for the study. Approximately 50% of the measurements have been completed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/082		<b>Status:</b> Suspended	
<b>Title:</b> Comparison of Sterile Isotonic Saline, Purified Water, and Dilute Hypochlorite Solution on the Rates of Infection and Tissue Response in Open Fractures of a Syrian Hamster Model					
<b>Start Date:</b> 03/24/95			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Randall K. Hildebrand, MC					
<b>Associate Investigators:</b> MAJ Mark D. Brissette, MC			LTC Frederic L. Johnstone, MC		
<b>Key Words:</b> Fractures, saline, purified water, hypocholorite, infection, tissue response,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

Study Objective: 1) To compare different irrigating solutions and rates of infection in an open fracture model. 2) To compare the gross and histologic effects in wound healing of an open fracture model after different irrigation solutions.

Technical Approach: A total of 48 syrian hamsters will be used in a 4 groups of 12. There will be 3 treatment groups and one control group. After adequate anesthesia, an incision on a hamster's leg will be made and the thighbone will be broken with a small power saw. The animals will be deliberately infected, and the treatment group animals will have the wound washed out with one of several kinds of irrigating fluids (sterile isotonic saline, purified water, or dilute hypochlorite solution). The animal will be awaked from anesthesia and returned to a recovery cage to be monitored for pain or infection. Two weeks later it will be euthanized. The rates of infection will be compared and the tissue around the wound will be examined under a microscope to determine any potential harmful effects of the infection or irrigation fluid.

Progress: There was a 95% infection rate at the time of harvest regardless of the irrigation technique used. Many of the animals grew multiple organisms, which indicates either intraoperative contamination or, more likely, postoperative contamination in the housing. There were other organisms present upon culture, but most of it was the original infective organism. To address these issues the investigator requested 20 additional animals in order to perform a dose response curve. An addendum to the original protocol was submitted to the LACUC. The addendum was tabled because the LACUC felt that more revisions should be made. The PI was then transferred to a new duty station. The protocol has been suspended until a new investigator has been appointed and until the additional revisions can be submitted and approved by the LACUC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/142		<b>Status:</b> Terminated	
<b>Title:</b> Cost Effectiveness of Screening MRIs of the Shoulder Prior to Neer Acromioplasties					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Randall K. Hildebrand, MC					
<b>Associate Investigators:</b>			LTC John D. Pitcher Jr., MC		
<b>Key Words:</b> acromioplasty, MRI, cost effectiveness					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** 1. To determine the sensitivity (SN), negative predictive value (NPV), and positive predictive value (PPV) and accuracy of shoulder MRIs in predicting rotator cuff tears of the shoulder. 2. To determine whether screening shoulder MRIs in patients with impingement syndrome is helpful and cost effective in the surgical management of preoperative management of those cases that are refractory to non-operative treatment.

**Technical Approach:** This is a prospective, single-blinded study of MRI vs operative evaluation, comparing their abilities to diagnose rotator cuff tears and other pathology about the shoulder. Patients selected for this study will have met the surgical indications for a modified Neer Acromioplasty for impingement syndrome with or without a suspected rotator cuff tear.

One hundred patients will have an MRI of the affected shoulder within two weeks of the anticipated subacromial decompression. MRI interpretation will be in the form of a radiological report documenting the presence or absence of rotator cuff tears or tendonitis, glenohumeral labral pathology, or other pathology about the shoulder. Intraoperatively the surgeon will record his findings both before and after review of the MRI and the MRI report. However, he will remain blinded to the MRI results until a surgical course has been decided intraoperatively. In other words, the surgery will begin as if no MRI had been performed. After an operative diagnosis and treatment course planned, the MRI and its report will be reviewed. If indicated by the MRI, the planned treatment course will be altered intraoperatively. Any and all treatment alterations based on the MRI will be recorded, and correlations will be made between pathology on surgical observation and those seen on the MRI.

Using open acromioplasty as the gold standard, after 100 surgeries the data will be reviewed to determine the SN, SP, NPV, and PPV, and accuracy of MRI. The need for preoperative MRI will be assessed by determining whether and how many operative plans are affected by the MRI and its interpretation.

**Progress:** No patients were entered and it has been terminated. This protocol was never started due to logistical problems between Orthopedics and Radiology.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/102		<b>Status:</b> On-going
<b>Title:</b> Teaching Program for Practical Microsurgery Using A Rat (Rattus norvegicus, strain HSD) As a Teaching Model				
<b>Start Date:</b> 03/24/95		<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> Surgery/Orthopedic		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Frederic L. Johnstone, MC				
<b>Associate Investigators:</b> LTC D. E. Casey Jones, MC		CPT Vernon S. Esplin, MC		
<b>Key Words:</b> Microsurgery:training, rat model,Animal Study				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		06/21/96

Study Objective: This teaching protocol will establish a formal training program in clinical microsurgery for orthopedic residents at MAMC. It will provide microsurgery practice in the repair of small vessels, nerves and tendons of the rat which model those of the hands, face and other body parts of humans.

Technical Approach: One rat will be used per week for 52 weeks for continuous microsurgery training for orthopedic residents. The rats will be placed under general anesthesia, used for numerous practice repairs and then humanely euthanitized at the conclusion of the surgical procedures. Specifically, the femoral artery of the rat serves as an excellent model of small human vessels and will be repeatedly cut and repaired. Residents will be tested after six weeks by oral examination and should be capable of performing extremity revascularizations.

Progress: One rat was used during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/128		<b>Status:</b> Terminated	
<b>Title:</b> Use of Pulsing Electromagnetic Fields to Potentiate Healing of Traumatic Combat and Training Injuries					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Dec 97		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC D. E. Casey Jones, MC					
<b>Associate Investigators:</b>			LTC Richard A. Sherman, MS		
MAJ Richard T. Dombroski, MC			Antje F. W. Goeken, Psy.D.		
Estelle Hamblen, BA, MHA			Melissa Wong, BA		
MAJ Kirk Willard, MC					
<b>Key Words:</b> Pulsing electromagnetic fields, injuries:combat, injuries:training					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** The overall objectives of the program are to determine whether pulsing electromagnetic fields (PEMFs) can be useful in potentiating recovery from combat wounds and training injuries when used in conjunction with standard techniques by (1) increasing the rate of healing while reducing swelling after hand, anterior cruciate ligament (ACL), and foot surgery or simple fractures of the long bones faster and further than standard techniques and (2) reduce the recovery time after stress fractures and ACL-related knee pain.

**Technical Approach:** This project is designed to determine whether exposure to PEMFs can potentiate healing of (a) traumatic combat and (b) training injuries including wounds, stress fractures, sprains, and ACL tears. These are representative of the types of injuries commonly seen in both combat and training. It is part of a program designed to prevent, track, and treat extremity trauma and training injuries among combat soldiers which should result in less loss of time away from the unit. It is the successor to the MRDC-funded project entitled "Use of body surface heat patterns for predicting and evaluating acute lower extremity pain among soldiers" (MRDC #8913004). We intend to study at least 40 subjects of each treatment/injury group. The major variables to be studied are (1) reduction of swelling and (2) increase in the rate of healing. The data will be analyzed separately for hand surgery, foot surgery, ACL repair, and long bone fractures with sub-types co-varied. The pre-surgical baseline measurements of swelling will be compared with daily measurements and the operated extremity will be compared with the intact extremity using a two way, repeated measures analysis of co-variance.

**Progress:** Six patients were entered in this study prior to FY 97. However, funding was not received from the grant application and investigators could not complete the study without additional technical support.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/155	<b>Status:</b> On-going
<b>Title:</b> Establishment of the Natural History/Progression of Pediatric Fingernail Injury Outcomes		
<b>Start Date:</b> 07/21/95	<b>Est. Completion Date:</b> May 97	
<b>Department:</b> Surgery/Orthopedic	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC D. E. Casey Jones, MC		
<b>Associate Investigators:</b> CPT George K. Bal, MC		CPT James T. Vandenberg, MC
<b>Key Words:</b> Fingernails, pediatric, injuries, natural history		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To establish the natural history of fingernail injury outcomes in children (1-8 years of age) with and without any distal phalanx fractures treated in the MAMC Emergency Department. To determine whether there is a need for follow-up studies on treatment procedures designed to reduce permanent abnormalities in the nails.

Technical Approach: Trauma is a major cause of pediatric fingernail injuries. In children, traumas may result in hematoma formation or nail avulsion. When the nail matrix and bed are unaffected, the effects are temporary. If the matrix or nail bed is injured, permanent scarring of the nail may result. Among adults, long term effects of trauma may include scarring and dystrophy of the nail if early treatment is not initiated.

Fifty children with fingernail injuries will be studied. Parents of the children meeting the entry criteria will be asked to participate. The child's injury will be assessed and photographed at the time of injury, and at followup visits at six week intervals for six months. A rate of abnormal healing will be determined and associated with cause and severity of the initial injury.

Progress: 7 subjects were entered during FY 97, for a total of 40 subjects.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/125		<b>Status:</b> On-going	
<b>Title:</b> External Fixation of Displaced Clavicle Fractures					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Aug 99		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Greer E. Noonburg, MC					
<b>Associate Investigators:</b>			LTCR Clayton E. Turner, MC		
<b>Key Words:</b> Clavicle fractures, external fixation					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** Determine the efficacy of external fixation in the treatment of clavicle fractures with greater than 100% displacement.

**Technical Approach:** Patients will be drawn from males and nonpregnant females over age 18, with acute traumatic clavicle fractures having greater than 100% displacement on radiographs. The study population will range from 10 to 20 subjects. After inclusion in the study, and a pre-operative examination, the subjects will be taken to the operating room for placement of threaded pins through four 1-cm incision sites over the clavicle. An Orthofix Pennig II External Fixator will be attached to the pins and the fracture reduced to as close as possible to anatomic alignment. After surgery, the patient will be given pain medications, instructed in pin site care, and sent home. The patient will be evaluated weekly by an orthopaedic surgeon (4-8 weeks) and usually will receive clavicle x-rays with each appointment. The external fixator will be removed in the clinic in four to eight weeks, depending upon healing of the fracture as evident on x-ray. Subsequent post-operative exams at 3, 6, and 12 months will be conducted. Outcome variables will be evaluated for functional outcomes (motor strength, range of motion, tenderness at the fracture site, residual displacement/deformity, time of healing, ability to perform occupation and activities of daily living).

**Progress:** 2 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/111		<b>Status:</b> Completed	
<b>Title:</b> Economic Evaluation of Scotchcast Plus vs Plaster of Paris for Immobilization of Fracture of the Arm and Leg					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Oct 96		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC John D. Pitcher Jr., MC					
<b>Associate Investigators:</b> Tim Davies			LTC D. E. Casey Jones, MC Ron Hawkinson		
<b>Key Words:</b> Casts, plaster of Paris, Scotchcast Plus					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** The objective of this study is to determine whether the inhalation of a helium-oxygen mixture (heliox) will improve pulmonary function and respiratory clinical status in adults hospitalized with severe asthma.

**Technical Approach:** We plan to enroll 15 subjects in this randomized, double blind, prospective, crossover study. Patients between 18-75 years of age admitted to the hospital for treatment of asthma will be asked to participate. The patients will be stabilized, and baseline pulmonary function tests, clinical score, heart rate, and pulsus paradoxus will be recorded. They will then be randomized to inhale either 30% oxygen-70% helium gas mixture or 30% oxygen-70% nitrogen (oxygen enriched air) first. After breathing the first gas via a face mask for 20 minutes, pulmonary function testing, assessment of clinical score, pulsus paradoxus and the other measurements will be repeated again. After a 10 minute period patients will then breath the second gas mixture for 20 minutes, and all the measurements will be repeated. After stopping the second gas mixture patients will rest for another 20 minutes, and all measurements will be measured for a 4th and final time. The patients, their families and all health care professionals with the exception of the respiratory therapist will be blinded to the order of administration of the two treatment regimens. Differences in continuous variables (i.e. FEV<sub>1</sub> and heart rate) will be analyzed with the two sample Student t-test, and difference in clinical scores (mean) will be assessed with the Wilcoxon rank sum test.

**Progress:** Approximately 22 subjects were studied. The fiberglass casts were less costly than the plaster.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/092		<b>Status:</b> On-going
<b>Title:</b> A Prospectively Randomized Study on the Effectiveness of Post-Operative Knee Bracing for Anterior Cruciate Ligament Reconstruction				
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> May 99	
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick St Pierre, MC				
<b>Associate Investigators:</b>			CPT Michael E. Kirk, MC	
<b>Key Words:</b> Anterior cruciate ligament:reconstruction, bracing				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** The objective of this study is to compare the effect of different post-operative brace patterns on the final outcome of an anterior cruciate ligament reconstruction. This will be performed by prospectively randomizing patients into two different bracing groups and comparing them with subjective and objective testing during their rehabilitation period.

**Technical Approach:** In summary, the present knowledge on post-operative bracing for ACL reconstruction is limited. This study is designed to determine if post-operative bracing has an effect on the outcome of an ACL reconstructed patient. A total of 80 patients will participate in the study. After arthroscopically assisted ACL reconstruction patients will be randomized to two study groups. Group A will wear a knee immobilizer for three weeks after surgery followed by no protective bracing for the remainder of their rehabilitation. Group B will wear a Don-Joy IROM brace locked at 0° for three weeks followed by three weeks in the brace with flexion set to 10° less than maximum flexion. At six weeks, the patient will wear a Don-Joy off-the-shelf functional knee brace daily for six months and for vigorous activities after that for at least the first year. Data collected at one, two, six, twelve, and 24 months will include range-of-motion, Lachman, anterior drawer and pivot shift-tests, as well as thigh circumference measurements. In addition at the six, twelve and 24 month follow-up visits, KT-100, LIDO, Lysholm and IKDC tests will be administered. A significant difference in the stability or functional assessment scores would indicate superiority of one method over the other regardless of cost. If both treatment groups are found to be equivalent, the most cost effective treatment method would be without bracing.

**Progress:** 50 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/086		<b>Status:</b> On-going
<b>Title:</b> A Prospectively Randomized Trial of Rotator Cuff Repair to Cortical Bone versus A Cancellous Trough				
<b>Start Date:</b> 03/15/96			<b>Est. Completion Date:</b> Apr 99	
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick St Pierre, MC				
<b>Associate Investigators:</b> CPT Roger W. Dougherty, SP			Hollis Potter, M.D.	
<b>Key Words:</b> Rotator cuff, cortical bone, cancellous trough,				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	03/21/97	

**Study Objective:** To determine if tendon repair to a cancellous trough is necessary for rotator cuff repair in humans.

**Technical Approach:** Forty patients with proven rotator cuff tears will be randomized to two surgical groups. Group A will have their rotator cuff tendon repaired to the greater tuberosity after a trough is made in the greater tuberosity of the humerus. Group B will have their rotator cuff repaired to the cortical bone of the greater tuberosity of the humerus without the creation of a trough. A thorough debridement of soft tissue to include bursa and scar will be performed in both groups. Postoperative treatment will be the same for each group. Clinical evaluations and physical exams to include range-of-motion, shoulder impingement signs and tenderness will be performed at one, six, twelve and twenty-four month follow-ups by the physical therapist department. The modified Hospital for Special Surgery (HSS) Score as well as an analog pain, function, and satisfaction score will be used for clinical evaluation. A significant difference in the assessment of strength scores would indicate superiority of one method over the other. MRI evaluations will be performed at six, twelve and twenty-four months. The MRI will be evaluated by an MRI radiologist at the HSS in New York City, New York, who will be blinded to the method of treatment for each patient. Criteria for success by MRI has been established by a recent study performed at the HSS by the radiologist and the principle investigator.

**Progress:** 6 subjects have been entered in FY 97, for a total of 7 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/174		<b>Status:</b> Terminated	
<b>Title:</b> Comparative Effectiveness of (a) Standard Treatment, (b) Standard Treatment Plus Force Measured Orthotic Cutting Methodologies, (c) Standard Treatment Plus Pulsing Electromagnetic Fields, and (d) A ..					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Orthopedic			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Kirk Willard, MC					
<b>Associate Investigators:</b>					
LTC Richard A. Sherman, MS			CPT Stephen Wilkerson, DPM		
Philip Block, DPM			John Gonzales, CPO		
Kimberly A. Hermann-Do, BS, MHA			Estelle Hamblen, BA, MHA		
Melissa Wong, BA			Linda Robson, BA		
<b>Key Words:</b> Ulcers:lower limbs, ulcers:feet, pulsed electromagnetic fields					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To compare the effectiveness of (a) standard treatment plus placebo pulsing electromagnetic fields (PEMFs), (b) standard treatment plus force measured orthotic cutting methodologies, (c) standard treatment plus PEMFs, and (d) a combination of all three for treatment of stable, open ulcers on the lower limbs and feet.

**Technical Approach:** We propose to perform a double-blinded study utilizing metabolically abnormal patients (mostly diabetic) with skin ulcers on their feet and lower legs which have not healed during the previous three months. Participants will be stratified by age, grade of ulcer, diameter of ulcer, and location of ulcer. Patients will then be randomized to one of the four groups described above. During the initial evaluation, all patients will be evaluated for pressure/force patterns and for blood flow to the ulcer. All patients, except those in the orthotics only group, will receive real or placebo PEMF therapy for five days per week for one hour per day until the ulcer heals or six weeks of treatment. Rate of ulcer healing will be measured by photography and videothermogram. Foot pressure patterns produced while standing still and walking will be measured at each evaluation session using automated pressure sensors set to average the pressure at each square cm of the sole. A power analysis of the pilot results shows that 33 subjects will be needed in each group assuming that we predict the PEMF/orthotic group will do better (one-tailed test) and an 80% chance of finding a difference between the four groups at a 0.05 level of significance. A total of 150 subjects will have to be started to account for dropouts. The data will be analyzed using a repeated measures analysis of variance.

**Progress:** This protocol was terminated because it was not funded. No patients were entered.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/099	<b>Status:</b> On-going
<b>Title:</b> Tendon-Healing to Cortical Bone After Tendon Reattachment Using Suture Anchors. A Biomechanical and Histological Evaluation in Goats		
<b>Start Date:</b> 04/25/97	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery/Orthopedic	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Robert V. Williamson, MC		
<b>Associate Investigators:</b> MAJ Ronald E. Nielsen, VC		MAJ Patrick St Pierre, MC
<b>Key Words:</b> Tendon healing, cortical bone, suture ahcnors, goat model, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** To examine the biomechanical properties and histological appearance of the bone-tendon interface after rotator cuff tendon repair of the shoulder in goats. The tendon will be reattached directly to the outer surface of the bone (i.e. cortical bone) using four different types of commercially available suture anchors for fixation. This will test if the anchor properties have any effect on healing of tendon to bone after surgical repair.

**Technical Approach:** An experimental model using the infraspinatus tendon in goats for evaluation of tendon repair has been established. 36 adult (3-5 years old) goats, *Capra hircus*, will be treated with bilateral tenotomy and subsequent reattachment of the infraspinatus tendon. Each test goat will have different types of suture anchors used on contralateral shoulders. The study endpoint will be at six and twenty-six weeks following operative repair. A total of 40 animals will be assigned by randomized block design to the timing and sequence of the operative techniques, the types of fixation, and for biomechanical, histological or control testing. (e.g. The first animal may be randomized to have anchor #1 used in the left shoulder and anchor #4 used in the right. It may be randomized to the histological group. The second animal may be randomized to have anchor #2 used in the left shoulder and anchor #3 used in the right. It may be randomized to the biomechanical testing at 26 weeks). Thirty-six animals will be used for biomechanical testing and four for histological analysis. By performing bilateral procedures in the same animal, we will be able to use pairing to compare different methods of fixation. This increases the statistical power of the study and reduces the number of animals needed.

**Progress:** Study has not yet begun.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY,  
OTOLARYNGOLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/157		<b>Status:</b> On-going
<b>Title:</b> Clinical Investigation of Viewpoint in Image-Assisted Surgery				
<b>Start Date:</b> 08/16/96			<b>Est. Completion Date:</b> Sep 97	
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Charles V. Edmond Jr., MC				
<b>Associate Investigators:</b> LTC Dianna Chooljian, MC			LTC Richard F. Debo, MC Michael McFarland	
<b>Key Words:</b> Viewpoint, 3-D digitizer, surgery, planning, localization, sinusitis				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: The objective of this study, to be conducted pursuant to this protocol, is to assess the spatial accuracy and reproducibility of fiduciary and anatomic registration in patients who are undergoing functional endoscopic sinus surgery, with the Viewpoint workstation.

Technical Approach: The viewpoint workstation is a computer assisting device designed to aid the surgeon in navigation and localization in 3 dimensions. The overall registration accuracy in representing real time surgical anatomy will be evaluated. Fifteen study patients will be enlisted from the Otolaryngology Clinic who demonstrate a clinical need for sinus surgery. During the patient preparation and operative procedure, the patient will undergo 3 separate measurements using the Viewpoint probe in order to assess fiducial registration accuracy and reproducibility. In addition, anatomic registration accuracy will be assessed and compared with the accuracy of fiducial registration. The data will be evaluated using the average standard deviation with 95% confidence intervals for the registration accuracy over the course of surgery.

Progress: The protocol has not started because the MAMC investigators needed changes made to both the hardware and the software in order to perfect the technique. To date, manufacturers have not agreed to make the required changes. Discussions are on-going with the manufacturers to try to reach some agreement in this area.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/177		<b>Status:</b> On-going	
<b>Title:</b> ENT Surgical Simulator Project					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Charles V. Edmond Jr., MC					
<b>Associate Investigators:</b>					
Doug Sluis, Ph.D.			Dale Fawcett		
Bill Winn, Ph.D.			Suzanne Weghorst		
Don Stredney			Blake Hanaford, Ph.D.		
Gregory J. Wiet, MD			Roni Yagel, Ph.D.		
			Bill Bolger, MD		
<b>Key Words:</b> Simulator:surgical, Simulator:ENT					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		9/30/97	

**Study Objective:** To develop and evaluate a minimally invasive prototype surgical simulator to establish real time fidelity requirements for tactile feedback and computer image synthesis.

**Technical Approach:** This project is a two phase program with the goal of Phase I to construct a simulator prototype to serve as a platform for further enhancement and evaluation. This includes the development of the geometric and virtual database of the human sinus anatomy, the development of a system to track the surgical instruments, and the system software to implement sinuscope camera emulation and tissue dissection. The prototype will provide the novice with the ability to perform a limited sinus surgery procedure on a virtual patient using sinuscope and surgical tools similar to those used in the operating room. Visual recognition skills and psychomotor skills specific to the surgical context are improved through the experience of the simulated surgery.

In Phase II, development will continue by enhancing the simulator to include changes and enhancements suggested by surgeons in the Phase I evaluation. Additional features such as tactile feedback and tissue deformation will be integrated into the prototype as time and budget permit. During Phase II further analysis will determine the simulators training effectiveness in operation.

**Progress:** During the course of this cooperative agreement, the research team built a real-time, man-in-the-loop, sinus surgery simulator. The simulator underwent months of evaluation. Preliminary formative evaluation results yielded suggestions for simulator enhancement. Where possible, the team implemented these suggestions. More rigorous summative evaluation efforts measure and document a statistically significant correlation between simulator scores and endoscopic surgical experience. This research is an important step in the technological evolution of surgical simulation in virtual reality training environment. It coincides with the Army's quest for training that maximizes the use of emerging technologies in computer simulation and virtual reality. Work will continue to improve the simulator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/134		<b>Status:</b> Completed
<b>Title:</b> Universal Screening of Hearing Loss Using Transient Evoked Otoacoustic Emissions				
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Aug 96	
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Theodore J. Kanne, MC				
<b>Associate Investigators:</b> Lynne A. Schaefer			MAJ Jonathan A. Perkins, MC COL David G. Schall, MC	
<b>Key Words:</b> Hearing loss:newborns, transient evoked otoacoustic emissions				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

**Study Objective:** First, to review the results of a universal screening program for hearing loss in newborns, which uses Transient Evoked Otoacoustic Emissions (TEOAE's) as a primary screening modality. From this data, hearing loss prevalence in this population will be determined. Secondly, to estimate the sensitivity, specificity, and predictive value of TEOAEs in identifying hearing loss in this study population. Finally, to analyze the cost-effectiveness of hearing screening with TEOAEs as compared to traditional audiometric screening methods.

**Technical Approach:** In this investigation, we will retrospectively review the outcome of a universal hearing screening program for newborns which includes the use of TEOAEs. The results of TEOAE screenings of 2200 infants born at MAMC since April 1995 will be reviewed. Those subjects who failed on initial TEOAEs and required retesting will be investigated by retrospective review of their medical records and secondary audiologic testing. This data will be used to estimate the incidence of hearing loss in this population as well as help determine its etiology (s). It will assist in the determination of the relative specificity and sensitivity of otoacoustic emissions as compared to the current methods with auditory brainstem response and behavioral audiometry. Our result will be compared to that found in the literature. A thorough cost-analysis profile regarding universal hearing screening with TEOAEs will be generated.

**Progress:** The medical records of 2300 patients were reviewed. The data indicated that Transient Otoacoustic Emission is an Effective screening modality for looking for occult hearing loss in infants. However, the incidence of hearing loss in our population was low enough to make justification of universal screening difficult. The incidence of risk factors for hearing loss in the study group was also quantitated.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/040		<b>Status:</b> Completed	
<b>Title:</b> The c-myc and int-2 Oncogenes in Extracapsular Spread of Lymphatic Metastasis in Head and Neck Squamous Cell Carcinomas					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Nov 95		
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Glen J. Mesaros, MC					
<b>Associate Investigators:</b> MAJ Charles V. Edmond Jr., MC			MAJ Rodger K. Martin, MS CPT Dale T. Waldner, MC		
<b>Key Words:</b> Cancer:head and neck, oncogenes					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To identify cases of oral cavity and oropharyngeal Squamous Cell Carcinoma (SCCA) from the Madigan tumor registry with N0,N1 without extracapsular spread, and N1 with extracapsular spread pathology. To utilize PCR technology in the retrospective genomic and gene product examination of oral cavity, oropharyngeal and nasopharyngeal SCCA. To correlate the amplification and expression of *c-myc* and *int-2* oncogene with the development of extracapsular lymphatic spread of oral cavity and oropharyngeal SCCA.

**Technical Approach:** The goal of this study is to determine whether or not an association exists between amplification and/or expression of *c-myc* and *int-2* with the presence of extracapsular spread of tumor outside the involved lymph node. The MAMC tumor registry will be searched for all tumors involving the oral cavity, oral pharynx, and hypopharynx. Specimens will be limited to 1989-1994, formalin fixed and paraffin embedded specimens which show nodal neck metastasis. A comparable number of primary tumors showing no nodal metastasis will also be incorporated and matched as to clinical staging parameters with those tumors having evidence of nodal disease. The pathology reports will then be pulled and those tumors showing extracapsular spread of tumor outside the lymphatics will be sub-categorized. The total of all specimens will be 50. The specimen blocks will be pulled, sectioned and individually reviewed by the Department of Pathology to confirm the diagnosis of SCCA and the presence or absence of extracapsular spread. Primers for mRNA PCR analysis will be derived from sequence analysis of the *c-myc* and *int-2* genes. Since these genes are not normally expressed in differentiated, non-proliferating cells, the demonstration of the expression of these two genes would be consistent with the previous findings in SCCA. If significant correlation is found between presence of the oncogene transcripts (proof of expression) and extracapsular spread, the relationship between extracapsular spread and over- expression of these genes will be explored.

**Progress:** Twenty-four tumors were reviewed. No significant difference was found in the expression of either oncogene (*c-myc* and *int-2*) between the specimens with extracapsular spread and the ones without.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/075		<b>Status:</b> Terminated
<b>Title:</b> Recurrent Acute Otitis Media: Treatment and Outcomes				
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Feb 02	
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Jonathan A. Perkins, MC				
<b>Associate Investigators:</b> COL Chung J. Jung, MC Lloyd D. Fisher, Ph.D. Ramsey Alsarraf, M.D.			George A. Gates, M.D. COL David G. Schall, MC Susan Norton, Ph.D.	
<b>Key Words:</b> Otitis media, antimicrobial prophylaxis, tympanostomy tube, adenoidectomy				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
			\$0.00	02/21/97

**Study Objective:** (1) To compare the outcomes of three randomly assigned treatments: a) medical prophylaxis, b) tympanostomy tube (TT) insertion, and c) adenoidectomy (A) plus TT (ATT) in young children with documented, multiple episodes of acute otitis media with effusion (AOME). The comparison will be in terms of a) the number of new episodes of AOME, b) clinical severity of new episodes using a new, disease-specific clinical evaluation scale, c) time with middle ear effusion (MEE), d) time with hearing loss, e) number of re-treatments, and f) number and type of complications of therapy over a three year follow-up period. (2) Compare the outcomes of the three treatments of recurrent AOME above in terms of new scales of functional health status and otitis-specific functionality, resource utilization, cost per unit reduction in otitis episodes, and standard measures of language, cognition, and social development.

**Technical Approach:** This application proposes a prospective, controlled, partially-blinded randomized clinical trial with three arms: 1) antimicrobial agent, with or without corticosteroid, 2) tympanostomy tubes (TT), and 3) adenoidectomy (A) + TT. Subjects are children from 12-36 months of age with a history of two or more episodes of AOME who are then entered into a pre-study observation phase. Those who experience a total of 4 episodes of AOME in the prior 12 months, at least one of which is documented during the observation period by the study team, will then undergo a complete medical evaluation. If no exclusion conditions are identified and if informed consent is given, the child is enrolled into the clinical trial. Each child is randomly assigned to one of the three groups, receives treatment and is observed at intervals during a three year follow-up phase. At the end, a comprehensive assessment of his or her otologic, audiologic, linguistic, cognitive, and social functional status is made. Follow-up intervals are 6 weeks in the first year, 8 weeks in the second year, and 12 weeks in the third year with intercurrent event visits at any time should symptoms suggestive of otitis media occur.

**Progress:** This project was terminated because the grant request was denied.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/044		<b>Status:</b> On-going	
<b>Title:</b> Pediatric Brochoesophagology Laboratory Using Swine (Sus scrofa)					
<b>Start Date:</b> 01/19/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Jonathan A. Perkins, MC					
<b>Associate Investigators:</b>			Andrew Inglis, M.D.		
<b>Key Words:</b> Brochoesophagology, swine model, pediatric,Animal Study					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		07/18/97

**Study Objective:** To familiarize the junior Otolaryngology residents at MAMC and the UW and the Pediatric surgery fellow at CHMC, with endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children.

**Technical Approach:** This is a 3-4 hour afternoon laboratory session. During this time, three pigs will be anesthetized under general anesthesia and rigid and flexible bronchoscopy and esophagoscopy will be performed by the course participants under the supervision of an attending endoscopist. Three separate stations will be used so a maximal number of procedures can be performed in the allotted time and the length of anesthesia is shortened. The first station will be for diagnostic flexible and rigid endoscopy. The second will be for tracheobronchial foreign body removal. The third will be for esophageal foreign body removal. A separate station will be used to teach endoscopic lasing techniques on prosected animal tracheal specimens. A morning lecture will be held on pediatric endoscopy prior to the laboratory and a quiz will be given over selected readings in pediatric endoscopy.

**Progress:** 3 pigs were used during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/002		<b>Status:</b> Completed	
<b>Title:</b> Experimental Model of the Palmaz Expandable Metallic Stent in the Trachea of Pigs (Sus scrofa)					
<b>Start Date:</b> 10/18/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Joseph L. Ruegemer, MC					
<b>Associate Investigators:</b> MAJ Kenneth S. Azarow, MC			MAJ Jonathan A. Perkins, MC MAJ Randall M. Holland, MC		
<b>Key Words:</b> Trachea, Palmaz stent, growth,Animal Study					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: 1. To observe effect of metallic stent in pig trachea on growth. 2. To develop an animal model capable of endoscopic evaluation of tracheal stenosis for subsequent studies assessing stent stability and manipulation in managing airway stenosis.

Technical Approach: Partial or complete obstruction of the trachea and main stem bronchi by congenital and pediatric airway anomalies present a challenging diagnostic and therapeutic problem to the otolaryngologist and pediatric surgeon. Definitive diagnosis requires endoscopic evaluation allowing direct visualization and location of the obstruction as well as dynamic assessment of the pediatric airway. Tracheobronchial malacia (narrowing) and stenosis, congenital and acquired, may progress to severe airway compromise and mandate aggressive intervention. Ideally, the treatment of choice involves surgical resection of the stenotic or malaciatic region with primary reanastomosis. This approach is acceptable for short stenotic segments, however not as feasible for more extensive lesions. In addition, major surgical procedures have inherently high associated morbidity and mortality. Currently, interest in using airway stents as alternative or adjunctive treatment of tracheal obstruction exists. Development of an animal model addressing basic questions such as effect on growth is needed in order to more fully evaluate the efficacy of airway stent utilization.

Progress: Nine pigs were studied. There was one death secondary to development of airway compromise followed by adverse anesthetic reaction. Stents were successfully placed and clinically tolerated by the majority of subjects. Animal weight gain was not adversely affected and tracheal diameter was increased in the stented subjects. In addition, histological evaluation of stented tracheal specimens were conducted using specific objective criteria and were reported. The piglet trachea proved to be a feasible model to evaluate stent use in airway stenoses.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/085	<b>Status:</b> On-going
<b>Title:</b> Immediate Extubation/Decannulation Following Laryngotracheoplasty Using Metallic Expandable Stents in the Pig ( <i>Sus scrofa</i> ) Airway		
<b>Start Date:</b> 04/25/97	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard W. Thomas, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth S. Azarow, MC	MAJ Jonathan A. Perkins, MC	
MAJ Larry K. O'Bryant, MC	CPT Ronald A. Gagliano, MC	
<b>Key Words:</b> Laryngotracheoplasty, stents, inflammation, granulation, extubation, decannulation, pig, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** 1) To develop a means of laryngotracheal reconstruction that will allow for the immediate extubation/decannulation of the surgically manipulated airway; and 2) to characterize the inflammatory reaction and granulation tissue formation following expandable metallic stent placement in the pig airway.

**Technical Approach:** A total of five pigs will be utilized for this study. As this is an exploratory process, two animals per group should suffice. Two pigs are necessary in the event of the loss of an animal due to unpredictable circumstances or complications. One animal will serve as a pilot study model to ensure that the initial airway control with immediate decannulation/extubation was performed as planned. A Palmaz balloon expandable metallic stent will be used; it is premounted with an unexpanded length of 30 mm and an internal diameter of 3.1 mm. The stent is comprised of a stainless steel tubular mesh. All pigs will be of the approximate same age and weight at the initiation of the study. The major endpoint will be any tissue reactivity following insertions of the stent into the airway of the animal.

**Progress:** This study, which used 4 animals, support the ability to perform airway surgery using expandable metallic stents in pigs and immediately decannulate postoperatively.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/084	<b>Status:</b> On-going
<b>Title:</b> Inflammatory Response Related to Tracheobronchial Distention in Pigs (Sus scrofa) Using Expandable Metallic Stents		
<b>Start Date:</b> 04/25/97	<b>Est. Completion Date:</b>	
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Richard W. Thomas, MC		
<b>Associate Investigators:</b>		
MAJ Kenneth S. Azarow, MC	MAJ Jonathan A. Perkins, MC	
MAJ Larry K. O'Bryant, MC	CPT Ronald A. Gagliano, MC	
<b>Key Words:</b> Tracheobronchial distention, stents, inflammation, pigs, Animal Study		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To characterize the inflammatory reaction and granulation tissue formation following expandable metallic stent placement in the pig airway.

Technical Approach: A total of five pigs will be utilized for this study. As this is an exploratory process, two animals per group should suffice. Two pigs are necessary in the event of the loss of an animal due to unpredictable circumstances or complications. One animal will serve as a pilot study model to ensure that the stent insertion and balloon expansion was accomplished as desired. A Palmaz balloon expandable metallic stent will be used; it is premounted with an unexpanded length of 30 mm and an internal diameter of 3.1 mm. The stent is comprised of a stainless steel tubular mesh. All pigs will be of the approximate same age and weight at the initiation of the study. The major endpoint will be any tissue reactivity following insertions of the stent into the airway of the animal.

Progress: This study, which used 5 animals, revealed graded inflammatory response in pig airways with airway stents.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/115		<b>Status:</b> Completed	
<b>Title:</b> Perioperative Management of the Obstructive Sleep Apnea Patient					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Surgery/Otolaryngology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith M. Ulnick, MC					
<b>Associate Investigators:</b>			LTC Richard F. Debo, MC		
<b>Key Words:</b> Sleep apnea, utilization of resources					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		9/30/97

**Study Objective:** 1) To determine the immediate (within 72 hours after surgery) complication rate for patients undergoing surgery of the upper airway to relieve or reduce the symptoms and complications associated with obstructive sleep apnea syndrome (OSAS). 2) Develop a guideline for the safe and cost effective management of obstructive sleep apnea patients in the postoperative period.

**Technical Approach:** A retrospective chart review will be conducted on all patients with the diagnosis of obstructive sleep apnea syndrome who have undergone an operation of the upper airway at this facility between 1 July 1992 and 30 June 1996. We will analyze the following data points; history and physical examination, social history from registration data, intraoperative documentation of fluids, complications, blood loss and procedure, postoperative physician/nursing notes, lowest SaO<sub>2</sub> while in the hospital, postoperative medications (pain, antibiotics, steroids, etc). Preoperative PSG to include Supine/Lateral RDI, Apnea Index (AI)/hypopnea index (HI), ECG, Sleep Efficiency and maximal SaO<sub>2</sub> desaturation. Analyze results to determine complication rate. After analyzing the data acquired, we should be capable of providing a more complete postoperative management guideline to effectively utilize the resources available at this institution.

**Progress:** Seventy-six charts were reviewed and 45 charts met the criteria. Initial findings indicate that the majority of patients can be monitored in the ACU post-operatively without compromising their care.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY,  
UROLOGY SERVICE**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/036		<b>Status:</b> On-going	
<b>Title:</b> Experience with the Dornier U50 Lithotripter					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ John B. Ellsworth, MC					
<b>Associate Investigators:</b>			MAJ Henry E. Ruiz, MC		
<b>Key Words:</b> Lithotripsy, renal calculi, ureteral calculi					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To determine the effectiveness (stone-free rate) and retreatment rate of the first Dornier U50 lithotripter in North America.

**Technical Approach:** The Department of Urology utilizes, via TRICARE contract, the newest lithotripter introduced into North America, at Allenmore Hospital, in Tacoma. All lithotriptors are compared to the Dornier HM3, water-immersed lithotripter, as the accepted gold standard. This new lithotripter is the Dornier U50, which provides an easy, tabletop approach to lithotripsy, utilizing a easily positioned treatment head which is coupled to a powerful shock-wave generator. Our goal is to determine the efficacy of this new lithotripter. We will review the procedure logbook at Allenmore Hospital and determine patients' inclusion or exclusion into this study. We then propose to review all reports of post-ESWL radiographs to determine the stone-free and retreatment rates of this machine.

**Progress:** Protocol is on-going. All records have received initial review and investigators are awaiting 90-day follow-up to determine if retreatment is required.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/014	<b>Status:</b> Completed
<b>Title:</b> A Retrospective Review of Vasovasostomy Using Loupe Magnification		
<b>Start Date:</b> 11/15/96	<b>Est. Completion Date:</b> Nov 96	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Kevin M. Feber, MC		
<b>Associate Investigators:</b> MAJ Henry E. Ruiz, MC		
<b>Key Words:</b> Vasovasostomy, Loupe Magnification		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: To complete chart review and describe the success rate of all patients receiving vasovasostomy performed with loupe magnification between 1990-1996.

Technical Approach: This study will determine the success rate of vasovasostomy performed with loupe magnification on all patients with available charts, who underwent this procedure at Madigan Army Medical Center between 1990 and 1996. Operator success will be judged by post-operative sperm concentration and sperm motility, while clinical success will be evaluated by successful conception post-surgery.

Progress: 160 subjects were studied. A patency rate of 87% and a 38% pregnancy rate were found. There was a 50% pregnancy rate in individuals who had less than a 5-year interval between vasectomy and vasovasostomy.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/104	<b>Status:</b> On-going
<b>Title:</b> Telomere Length and Telomerase Activity in Human Testicular Cancer		
<b>Start Date:</b> 06/16/95	<b>Est. Completion Date:</b> Jul 97	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC		
<b>Associate Investigators:</b>		
MAJ J. Brantley Thrasher, MC	CPT Wade K. Aldous, MS	MAJ Kenneth W. Westphal, MC
CPT Keith J. O'Reilly, MC	Troy H. Patience, B.S.	
<b>Key Words:</b> Cancer:testicular, telomerase		
<b>Accumulative</b> <b>MEDCASE Cost:</b>	<b>Est. Accumulative</b> <b>OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in tumorous testicular tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship, if any, between activity of telomerase and the stage and grade of testicular cancer.

**Technical Approach:** Tissue samples will be taken from 40 male patients undergoing surgical resection for testicular cancer. All malignant and benign tumor types resected during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into the telomere repeats on a known DNA primer. These will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric T-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired T-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress:** One subject was entered during FY 97, for a total of 3 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/097	<b>Status:</b> On-going
<b>Title:</b> Telomerase Activity in Voided Urine and Bladder Washings As A Diagnostic and Surveillance Marker for Transitional Cell Carcinoma		
<b>Start Date:</b> 05/16/97	<b>Est. Completion Date:</b> May 97	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC		
<b>Associate Investigators:</b>		
CPT Wade K. Aldous, MS	MAJ J. Brantley Thrasher, MC	
Kim NW	J. Balser	
Lynch S	Judd W. Moul, M.D.	
Kane C	LTC James P. Foley, CH	
<b>Key Words:</b> Cancer:transitional cell, telomerase, urine, bladder, washings		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** The objective of this study is to determine the sensitivity and specificity of telomerase activity in the voided urine and bladder washings of patients with bladder cancer as a diagnostic and surveillance marker. This will be compared to traditional cystoscopic examination.

**Technical Approach:** Bladder cancer remains a significant cause of cancer among both men and women in this country. Diagnosis and surveillance require invasive and often painful testing. Telomerase activity in the voided urine appears to be a promising non-invasive marker of bladder cancer. We seek to determine telomerase activity or its absence in the voided urine of 100 patients with newly diagnosed bladder cancer as well as approximately 200 patients at high risk for recurrence. We will compare these results to the telomerase activity in voided urine from 100 age matched, mixed gender subjects undergoing cystoscopy and found not to have bladder cancer. Data collected will include percentage of telomerase positive urine in the newly diagnosed bladder cancer group compared to the non-cancer control group. Furthermore the number of telomerase positive urine in patients with recurrent TCC in the group of patients at high risk for recurrent bladder cancer. Data will be analyzed to determine sensitivity, specificity, and positive predictive values.

**Progress:** 92 subjects were entered during FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 95/109	<b>Status:</b> Completed
<b>Title:</b> Telomere Activity and Expression of p53 and Rb in Human Transitional Cell Carcinoma		
<b>Start Date:</b> 04/21/95	<b>Est. Completion Date:</b> Jul 97	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC		
<b>Associate Investigators:</b> CPT Wade K. Aldous, MS      MAJ J. Brantley Thrasher, MC Troy H. Patience, B.S.		
<b>Key Words:</b> Cancer: bladder, telomere, temomerase		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** This study encompasses four objectives. To determine the presence or absence of telomerase activity in transitional cell carcinoma tissue and normal tissue. To observe the average telomeric length of both tissue types to compare differences in length, hypothesizing that tumor tissue would have shorter telomeres. To quantify telomerase activity in tissues with an active enzyme. To determine the relationship between activity of telomerase and the stage and grade of human transitional cell carcinoma.

**Technical Approach:** Tissue samples will be taken from 40 male and female patients undergoing operative resection for bladder cancer. All malignant and benign tumors of the bladder found during surgery will be investigated. Tissue from the tumor and from surrounding histologically normal areas will be transferred from the Dept. of Pathology to the Dept. of Clinical Investigation. Genomic DNA will be extracted from the tissues and subjected to *Rsa*I and *Hinf*I restriction digestion. The fragments will then be separated by agarose gel electrophoresis, Southern blotted, and detected by chemiluminescence using a digoxigenin-labeled telomere probe. These will be visualized by x-ray film exposure and will provide the composite lengths of all telomeres in a cell population. Actual telomerase activity in tumorous and normal tissue will also be measured by extracting the enzyme from tissues and assaying for activity *in vitro*. The positive control is an immortalized cell line. Activity is measured by the successful incorporation of radio-labeled dGTP nucleotide into telomere repeats on a known DNA primer. The modified primers will be separated on a polyacrylamide gel and quantified by densitography. The differences in telomere length will be tested by a non-parametric t-test. Chi-square analysis will be used to test for telomerase activity assuming normal tissue has inactive enzyme and tumor tissue has active enzyme. The paired t-test will be used to quantify telomerase activity compared to positive controls and a non-parametric ANOVA will be used to determine the correlation between the amount of activity and the stages and grades of tumors.

**Progress:** Telomerase activity was detected in 25/26 (96%) solid specimens, 21/26 (81%) bladder washing, and 6/11 (54%) voided urine specimens from patients with histologically confirmed transitional cell carcinoma. In the control group, 2/13 (15%) benign urothelial specimens and 2/56 (4%) voided urine specimens from the asymptomatic volunteer group demonstrated telomerase activity. Of those with benign urologic disease, 16/40 (40%) bladder barbotage specimens and 6/12 (50%) voided urine specimens demonstrated telomerase activity. Sensitivity and specificity of telomerase as a marker for transitional cell carcinoma in the bladder washings group was 81% and 96%, respectively, and 54% and 96% in voided urine, respectively. An unexpectedly high false positive detection rate in patients with benign urologic diseases, especially symptomatic BPH, was noted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/069		<b>Status:</b> On-going
<b>Title:</b> Vibratory Stimulated Bladder Cell Exfoliation in Voided Urine				
<b>Start Date:</b> 03/21/97		<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Raymond S. Lance, MC				
<b>Associate Investigators:</b> Kim NW		MAJ J. Brantley Thrasher, MC		
<b>Key Words:</b> Cancer:transitional cell carcinoma, RNA, bladder cell exfoliation, high frequency vibration				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: To determine the difference in the total RNA and cell count in voided urine specimens after 5 minutes of high frequency vibration to the suprapubic area compared to routine voided urine specimens.

Technical Approach: Freshly voided urine specimens will be obtained from 20 normal male and female volunteers and again collected after application of the bladder vibrator to the suprapubic area for 5 min. Additionally, we will evaluate 10 patients with micro or gross hematuria and 10 patients with known bladder tumors prior to transurethral resection. rRNA measurements before and after application of the vibrator will be compared to determine the difference in the total RNA as well as cell count.

Progress: 28 subjects were entered during FY 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/129		<b>Status:</b> On-going	
<b>Title:</b> The Correlation Between Free and Total PSA, Prostate Specific Membrane Antigen and Sex Hormone Binding Globulin Across the Spectrum of Prostate Disease					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith J. O'Reilly, MC					
<b>Associate Investigators:</b> MAJ J. Brantley Thrasher, MC Katherine H. Moore, Ph.D.			MAJ Raymond S. Lance, MC Murphy GP		
<b>Key Words:</b> Prostate specific antigen, SHBG, prostate disease					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To examine across the spectrum of prostate disease (normal to prostate cancer) whether there is a statistically significant correlation between the serum levels of the free and bound fractions of Prostate Specific Antigen (PSA), sex hormone binding globulin (SHBG), Prostate Specific Membrane Antigen (PSMA) and serum androgens.

**Technical Approach:** This study will evaluate men aged 45-80 and examine the serum levels of free and bound Prostate-specific antigen (PSA), sex hormone binding globulin (SHBG), Prostate-specific membrane antigen and serum androgens. The subjects will be divided into one of two arms: those with no evidence of prostate cancer and those with histologically proven adenocarcinoma of the prostate. All subjects will be patients who present to the urology clinic for urologic evaluation and will have one extra vial of serum drawn. The levels of these proteins will be examined for statistically significant correlation. By proving or disproving a relationship among these proteins and its variation across the spectrum of prostate disease a greater knowledge of the biochemistry of the prostate will be apparent and hopefully improve current diagnostic methods for detecting the presence or absence of prostate cancer.

**Progress:** 173 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/038		<b>Status:</b> Completed	
<b>Title:</b> Concomitant Use of the Erection Vacuum Device and Penile Prosthesis					
<b>Start Date:</b> 12/19/96			<b>Est. Completion Date:</b> Mar 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith J. O'Reilly, MC					
<b>Associate Investigators:</b>			CPT Rayford A. Petroski, MC		
CPT Bradley F. Schwartz, MC			MAJ J. Brantley Thrasher, MC		
CPT Douglas W. Soderdahl, MC					
<b>Key Words:</b> Penile prosthesis, erection vacuum device					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		9/30/97
			\$0.00		

**Study Objective:** To describe the safety and efficacy of the combined use of the erection vacuum device in patients with a previously placed penile prosthesis.

**Technical Approach:** Erectile dysfunction is a considerable problem affecting many diabetics and others with atherosclerotic disease and neurologic disorders. Therapy currently relies on evaluation of the underlying cause of the dysfunction and treatment of the underlying disorder. Unfortunately with the majority of patients, the cause is not reversible with treatment of the underlying disease. These patients are usually managed with an initial trial of intracavernous injection therapy or an erection vacuum device. If these prove unsatisfactory, an inflatable penile prosthesis or a malleable or semi-rigid penile prosthesis is placed surgically. A small percentage of patients find that their prosthetic erection is either lacking in length or girth, thus theoretically handicapping performance both physically and mentally.

**Progress:** Eight subjects were studied using the Rigi-Scan device in conjunction with the vacuum device. The data indicate that the use of the vacuum device is effective and safe for the augmentation of penile prosthesis in patients who are not pleased with the prosthesis. Increase in size and girth as well as patient and partner satisfaction has been shown.

The principal investigator was changed to Dr. O'Reilly from CPT Douglas Soderdahl in June 1997.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/129		<b>Status:</b> On-going	
<b>Title:</b> Oral Ciprofloxacin for Acute Prostatitis					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b> Apr 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Keith J. O'Reilly, MC					
<b>Associate Investigators:</b> CPT Bradley F. Schwartz, MC CPT Douglas W. Soderdahl, MC			CPT Rayford A. Petroski, MC MAJ J. Brantley Thrasher, MC		
<b>Key Words:</b> Prostatitis, cirpofloxacin, ampicillin, gentamicin, trimethoprim, sulfamethoxasole					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 06/20/97

**Study Objective:** To evaluate the efficacy of oral Ciprofloxacin (Cipro) in the treatment of acute prostatitis in comparison to traditional I.V. Ampicillin (Amp) and Gentamicin (Gent).

**Technical Approach:** The study population will consist of 50 men eligible for MAMC care who present with signs and symptoms consistent with acute prostatitis and meet entry criteria for inpatient treatment with either Cipro or IV Amp/Gent. Patients will be randomized to treatment with Cipro 500mg PO BID for 30 days or IV Amp (1gm q 6hrs)/Gent (5mg/Kg) followed by Trimethoprim/Sulfamethoxazole (Septra DS), one tablet PO BID, for a combined total of 30 days. Efficacy of treatment will be based on length of hospital stay, time to resolution of symptoms, time to defervescence and evaluation of complications. Patients will be followed up in 6-8 weeks after completion of outpatient therapy an will receive exams and laboratory tests according to the Stamey technique. Additional follow-up will be done at 6 and 12 months for recurrence or chronic states. Analysis of data will include chi-square, student t-test and ANOVA.

**Progress:** 11 subjects were entered during FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/136	<b>Status:</b> On-going
<b>Title:</b> The Protegen Sling for the Treatment of Female Stress Urinary Incontinence: A Pilot Study		
<b>Start Date:</b> 08/15/97	<b>Est. Completion Date:</b> Aug 99	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Henry E. Ruiz, MC		
<b>Associate Investigators:</b>		
LTC Leland D. Ronningen, MC	MAJ J. Brantley Thrasher, MC	
COL Gary D. Davis, MC	COL John C. Norbeck, MC	
CPT Jerome L. Buller, MC	MAJ Raymond S. Lance, MC	
CPT Keith J. O'Reilly, MC	MAJ John B. Ellsworth, MC	
Meyer K	CPT Karen C. Evans, MC	
<b>Key Words:</b> Urinary incontinence, protegen sling		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: 1) To determine the safety, efficacy and cost effectiveness of the Protegen sling; and 2) to determine the feasibility of using a minimally invasive technique to place the sling.

Technical Approach: Patients from the Urology and Gynecology Clinics with stress urinary incontinence who decide to have surgical treatment of their condition will be asked to participate in the study. All patients will undergo standard preoperative evaluation as previously described. The Protegen will be placed under spinal or general anesthesia, using a minimally invasive approach. Antibiotics will be used peri-operatively and post-operatively for one week. Follow-up will be scheduled at one week, 1,3,6,12 months, and yearly thereafter for a total of two years. At each visit the patient will have a history and physical examination, urinalysis and urine culture, number of pads used will be determined, urodynamics with leak point pressure measurement, uroflow and post void residuals will be done if clinically indicated. Safety, efficacy, and cost effectiveness will be assessed as previously described.

Progress: Protocol has not yet started pending approval of funding.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/158	<b>Status:</b> On-going
<b>Title:</b> Multi-center Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor Inflatable Penile Prosthesis		
<b>Start Date:</b> 08/16/96	<b>Est. Completion Date:</b> Oct 02	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Henry E. Ruiz, MC		
<b>Associate Investigators:</b> CPT Douglas W. Soderdahl, MC MAJ Raymond S. Lance, MC		
MAJ J. Brantley Thrasher, MC MAJ John B. Ellsworth, MC		
<b>Key Words:</b> Penile Prosthesis: Ambicor, Inflatable, Safety, Effectiveness		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	08/15/97

**Study Objective:** The primary effectiveness objective is to evaluate the ability of the AMS Ambicor inflatable penile prosthesis to provide an erection suitable for sexual intercourse (device function) as determined by physical examination and patient self-report. Secondary effectiveness objectives include estimating the effects of the prosthesis on patient sexual function and satisfaction, self-esteem, quality of life, and psychological well-being. The study will also evaluate levels of patient satisfaction with various aspects of the prosthesis including rigidity, length, girth and flaccidity. Safety will be evaluated by measuring rates of post implant complications (including device malfunction) and the occurrence of medical conditions.

**Technical Approach:** This is a multi-center, prospective, cohort study with the pre-implant experience of patients serving as the comparison for the evaluation of effectiveness and safety. The study sample will be derived from patients who present to the clinic with the diagnosis of erectile dysfunction. After an eligible patient makes an informed decision to be implanted with an AMS Ambicor penile prosthesis and signs the surgical consent he will be asked to participate in the study. A total of 250 patients will be recruited nationwide (12-20 being from MAMC) and will be implanted with the Ambicor inflatable penile prosthesis. The primary measure of effectiveness (sexual function, self-esteem, and psychological well-being), will be monitored for 2 years with visits at 6 weeks post-surgery, 6 months, 1 year, 18 months and 2 years. Follow-up for complications, associated medical conditions and other adverse device effects will be followed for 5 years with phone contact at 3 and 4 years, and a visit at 5 years.

**Progress:** 9 subjects have been entered in FY 97, for a total of 10 subjects.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/100		<b>Status:</b> Completed	
<b>Title:</b> Comparison of Five Second Urinary Home Flow Rates to Formal In-Office Uroflowmetry					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Douglas W. Soderdahl, MC					
<b>Associate Investigators:</b>					
MAJ J. Brantley Thrasher, MC		MAJ Henry E. Ruiz, MC CPT Bradley F. Schwartz, MC			
<b>Key Words:</b> Urinary flow rates, uroflowmetry, home flow rates					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

**Study Objective:** To determine if five second urinary home flow rates correlate with standard in-office uroflowmetry and maximum urinary flow rates. While it is difficult to analyze the costs of procedures performed in our clinic, the medicare reimbursement for in-office uroflows is \$78. The specimen cup in the confines of the private household will undoubtedly be less expensive.

**Technical Approach:** We will attempt to show that home five-second urinary flow rates in the evaluation of bladder outlet obstruction is as accurate and effective as formal in-office uroflowmetry, specifically maximum urinary flow rate ( $Q_{max}$ ). In addition, home flows will be less expensive and may perhaps be more "physiologic" in the sense that it is obtained in a more natural environment. Fifty five male subjects who seek urologic consultation for signs and symptoms of bladder outlet obstruction will be recruited. Patients will obtain five-second home urinary flow rates using a pre-measured cup, instruction sheet and blank form to document their flows. Flow rates will be obtained once daily for two weeks. They will then have in-office uroflow with uroflowmetry on three separate occasions. A power analysis determined that 55 patients would be required for a 2 cc/sec difference in modalities and 90% power. Data will be analyzed using the paired t-test.

**Progress:** Twenty patients were entered in FY 97 for a total of 60 patients. There was a slight difference, but not significant enough to warrant a change in methods.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/113		<b>Status:</b> On-going	
<b>Title:</b> Relief Strategies for Initiative Bladder Symptoms Associated with Intravesical BCG - A Pilot Study					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> May 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> William J. Ellis, M.D.			Donna L. Berry, Ph.D., RN		
<b>Key Words:</b> Bladder; oral hydration, dietary supplementation, potassium,sodium citrate, BCG					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		05/16/97	

**Study Objective:** The purpose of this pilot intervention study is to evaluate an oral hydration regimen and dietary supplementation with potassium/sodium citrate as relief strategies for irritative bladder symptoms associated with BCG intravesical therapy.

**Technical Approach:** This randomized, 2 X 2 pilot study is designed to investigate an oral hydration regimen and urinary alkalization with potassium/sodium citrate. Forty subjects, experiencing irritative bladder symptoms associated with intravesical bacillus Calmette-Guerin, will be randomized to either an oral hydration regimen, urinary alkalization with potassium citrate, a combination of the oral hydration regimen and urinary alkalization with potassium citrate, or usual clinical practices. The intervention will be applied for one week during week 4 of the intravesical treatment course. Urine pH will be monitored and symptoms will be measured using the Irritative Bladder Symptom Inventory. Symptom data will be analyzed using a two-way analysis of variance with a test for interaction.

**Progress:** 18 subjects have been entered in FY 97, for a total of 22 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/002		<b>Status:</b> Completed	
<b>Title:</b> Measurement of Irritative Bladder Symptoms					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> May 96		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> LTC Kurt L. Hansberry, MC			Donna L. Berry, Ph.D., RN		
<b>Key Words:</b> Cancer:bladder, irritative bladder symptoms					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** To test the properties of the Irritative Bladder Symptom Inventory (IBSI) in terms of: a) construct and content validity, b) internal consistency, and c) test-retest reliability in a sample of individuals receiving intravesical therapy for bladder cancer.

**Technical Approach:** Sixty individuals will be asked to complete the one-page, nine-item IBSI on the first day of intravesical treatment, prior to the instillation, and then each night prior to going to bed for 42 nights. This period includes the duration of intravesical therapy plus 7 days after the final installation. Validity will be examined and internal consistency will be assessed through extensive item and scale analyses. IBSI item analyses will include examination of item descriptive statistics, inter-item measures of association, scale mean, scale variance, and Cronbach's alpha. Test-retest reliability will be conducted at 1- and 2-week intervals. The findings will be used to establish the IBSI as a valid and reliable tool for monitoring irritative bladder symptoms.

**Progress:** Thirty one patients were entered on this study in FY 96. No further work was done on the study in FY 97. The investigators conclude that a daily administered version of the 9 items IBSI is a valid and reliable instrument for measurement of irritative bladder symptoms associated with BDTG intravesical therapy in men. The IBSI had acceptable reliability at times when patients were experiencing both minimum (before treatment) and maximum (week 4) levels of symptoms. The instrument must be tested further in women receiving intravesical therapy.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/130		<b>Status:</b> On-going
<b>Title:</b> Immunity in Prostate Diseases				
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Jun 99	
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b> Disis N			Cheever MA	
<b>Key Words:</b> Prostatitis, autoimmune				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
			<b>Periodic Review:</b> 9/30/97	

**Study Objective:** To determine whether patients with prostatitis have immunity to prostatic proteins.

**Technical Approach:** Serum on patients with presumptive autoimmune prostatitis will be examined for antibody immunity and T cell immunity to prostate proteins. If serum antibody responses to prostate proteins are detected, additional blood will be drawn to examine for T cell responses to prostate proteins. All patients with presumptive autoimmune prostatitis or patients with prostatitis of unknown origin will be eligible. Up to 100 patients will be studied, 50 with prostatitis and 50 controls. The presence or absence of serum antibody to prostate proteins will be determined by standard immunoblot methods. If antibody to prostate proteins is detected, the protein targets of autoimmune prostatitis will be identified by expression cloning, using standard methods.

**Progress:** This study has not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/164		<b>Status:</b> On-going
<b>Title:</b> Prostate Cancer Intervention vs Observation Trial (PIVOT): A Randomized Trial Comparing Radical Prostatectomy vs Palliative Expectant Management for the Treatment of Clinically Localized Prostate ...				
<b>Start Date:</b> 09/21/94		<b>Est. Completion Date:</b> Sep 04		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b>		LTC Kurt L. Hansberry, MC		
<b>Key Words:</b> Cancer:prostate, prostatectomy, palliative management				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	03/21/97	

**Study Objective:** To determine which of 2 treatment strategies is superior in reducing all-cause mortality in patients with clinically localized prostate cancer (1) radical prostatectomy and early intervention of subsequent disease persistence or recurrence or (2) expectant management with reservation of therapy for palliative treatment of symptomatic or metastatic disease progression.

**Technical Approach:** Patients will be randomized to one of the two groups listed (1) will have a radical prostatectomy; (2) will be assigned to Watchful Waiting Management.

Patients in group 1 will have 2 surgical procedures; removal of the lymph nodes from near the prostate gland (pelvic lymph node surgery); and then proceed with the prostatectomy.

Patients in group 2 will not have their cancer removed. Patients will be closely observed; if the cancer causes symptoms, treatment will be aimed at providing relief of these symptoms.

**Progress:** No subjects have been entered in FY 97. Subjects have been unwilling to be randomized.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/134		<b>Status:</b> On-going	
<b>Title:</b> Comparative Study of the Clinical Efficacy of Two Dosing Regimens of Eulexin: 250 mg Q8h vs 500 mg QD					
<b>Start Date:</b> 05/19/95			<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>			LTC Kurt L. Hansberry, MC		
COL John N. Wettlaufer, MC			CPT Douglas W. Soderdahl, MC		
MAJ Henry E. Ruiz, MC			COL John C. Norbeck, MC		
MAJ Raymond S. Lance, MC					
<b>Key Words:</b> Cancer:prostate, Eulexin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					08/15/97

**Study Objective:** To compare the clinical effectiveness of a new dosing regimen (500mg QD) for administering flutamide to the currently indicated dosing regimen of 250 mg QD according to (1) the percent of patients normalizing PSA and (2) quality of life differences between the two regimens.

**Technical Approach:** This phase IV, multi-center, open label, prospective randomization study will include 400 patients (10 from MAMC), ages 40 to 85, with clinically proven and histologically confirmed adenocarcinoma of the prostate gland. The subjects will be randomized to one of two treatment groups, Flutamide 250mg QD or Flutimade 500 mg QD, at Time 0. Time 0 is the day of surgical or medical castration. The study treatments will be continued for three months. The two variables to be evaluated are normalized PSA values as determined by standard laboratory PSA test, and quality of life as determined by questionnaire. Laboratory tests will be taken at clinic visits at Time 0, and weeks 4, 8, and 12. PSA normalization will be performed on 12 weeks data after the last patient accrued has reached the 12 week point. In order to achieve the conventional 80% power for showing equivalence, 200 patients per arm will be required based on a threshold criterion of 15%. Evaluation of the Quality of Life modules will involve multivariate analysis of variance for repeated measures for HQL domains and symptoms. Treatment by time interaction effect will be assessed under the repeated measures model to identify HQL domains that are significantly different between the two treatment arms using a two-sided 5% level test.

**Progress:** 14 subjects have been entered in FY 97, for a total of 30 subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/083		<b>Status:</b> Terminated
<b>Title:</b> Diet and Prostate Hormones				
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jul 95	
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b> Stephen R. Plymate, M.D.			Alan R. Kristal, Dr.P.H. Johanna Lampe, Ph.D.	
<b>Key Words:</b> Cancer:prostate, diet, prevention				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
				<b>Periodic Review:</b> 9/30/97

**Study Objective:** 1) To better understand the relationships of diet with prostate cancer.  
2) To evaluate the potential value of dietary change for the primary prevention or adjuvant therapy of prostate cancer.

**Technical Approach:** This study will recruit 10 men with newly-diagnosed, localized and histologically well-differentiated prostate cancer who elect to undergo prostatectomy. They will be randomized into two arms: 1) low fat (20%) and high fruit and vegetable (8+ servings/day) diet for 4-6 weeks before prostatectomy or 2) their usual diet. Dihydrotestosterone and Testosterone concentrations will be measured in blood, prostate biopsies, and prostate tissue removed at prostatectomy.

**Progress:** Six patients were entered. Most patients did not want to continue on the low-fat diet prior to prostatectomy. Therefore, the protocol was terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/147		<b>Status:</b> On-going
<b>Title:</b> Comparison of Quality of Life (QOL) Differences Between Radical Retropubic (RRP) and Radical Perineal Prostatectomy (RPP) for Clinically Localized Prostate Cancer				
<b>Start Date:</b> 10/17/97		<b>Est. Completion Date:</b> Sep 99		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b>		MAJ Raymond S. Lance, MC		
<b>Key Words:</b> Cancer: prostate, prostatectomy:retropubic, prostatectomy:perineal				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	9/30/97	

Study Objective: To determine QOL differences between patients undergoing RRP and those undergoing RPP for clinically localized prostate cancer.

Technical Approach: This study will prospectively evaluate and compare the QOL of male patients 30-80 years of age who undergo RRP and RPP for clinically localized carcinoma of the prostate. The study will utilize a validated questionnaire, the UCLA-RAND Prostate Cancer Index, administered to the patients (alone and without interruption) at least one week prior to the procedure and then at 1 month, 3 months, 6 months and 1 year postoperatively. This instrument will allow us to compare the effects of the 2 procedures on the patients' health-related QOL and eventually aid the urologist in choosing the appropriate approach for each patient.

Progress: New protocol has not been started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/150		<b>Status:</b> Completed
<b>Title:</b> Center for Prostate Disease Research Prostate Cancer Radical Prostatectomy Follow-up Questionnaire				
<b>Start Date:</b> 06/16/95		<b>Est. Completion Date:</b> Sep 95		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b>		Judd W. Moul, M.D.		
<b>Key Words:</b> Cancer:prostate, prostatectomy, questionnaire				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

**Study Objective:** The objective of this study is to conduct a comprehensive survey of men who have undergone a radical prostatectomy (RP) for prostate cancer (PC) to assess long-term quality of life (QOL) regarding impotence, incontinence and surgical complications.

**Technical Approach:** In 1994 there have been over 200,000 new cases of PC diagnosed in the United States, and the use of RP as a treatment modality has increased over 200% since the mid 1980's. With the increasing use of RP, more attention has focused on side effects and complications of the treatment and how they relate to overall QOL in these men. In a multicenter study (WRAMC and MAMC), a QOL questionnaire, regarding impotence, incontinence and surgical complications has been developed. This questionnaire will be mailed to subjects recruited from the database of all RP patients treated at MAMC and WRAMC between 1980-1994. A total of 400 returned questionnaires will be sufficient for data analysis. Most of the results will be descriptive statistics of morbidity percentages. Logistic regression will be used to model long-term quality of life outcome variables.

**Progress:** 111 patients were entered at MAMC. Despite significant rate of mild incontinence and impotence, the majority of patients would opt for radical prostatectomy again. Long-term problems with stricture are uncommon. The mean age of patients on this study was 63.5 years.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/120		<b>Status:</b> On-going	
<b>Title:</b> A Randomized, Double-Blind Study (With Open-Label Treatment Extension) to Evaluate the Efficacy and Safety of VIAGRA™ (Sildenafil) in Erectile Dysfunction					
<b>Start Date:</b> 07/18/97			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>			COL John C. Norbeck, MC		
LTC Leland D. Ronningen, MC			MAJ Henry E. Ruiz, MC		
CPT Douglas W. Soderdahl, MC			MAJ Raymond S. Lance, MC		
MAJ John B. Ellsworth, MC			CPT Keith J. O'Reilly, MC		
<b>Key Words:</b> Erectile dysfunction, VIAGRA, efficacy, safety, quality of life					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		9/30/97	
\$0		\$0.00			

**Study Objective:** To assess the efficacy, safety, quality of life, and patient and partner satisfaction over a 3 month period of oral administration of VIAGRA™(Sildenafil), as required, approximately one hour prior to sexual activity in male outpatients with erectile dysfunction.

**Technical Approach:** The study population will be male outpatients, 18 years of age and older, with well-documented history (>6 months) of erectile dysfunction of broad-spectrum etiology. The study design is a randomized, double-blind, placebo-controlled, parallel group, multicenter, flexible dose study. Patients will be randomized equally into either a placebo treatment group or a VIAGRA™ treatment group. All patients will commence at a dose of 50 mg of VIAGRA™(or corresponding placebo) and depending on efficacy, safety, and toleration, the dose may be increased to 100 mg or decrease to 25 mg, if necessary. Doses will be taken as required (not more than once daily) approximately 1 hour prior to anticipated sexual activity. The study will last 16 weeks for each patient (4 week run-in period and 12 weeks double-blind treatment). Patients who complete the 16 week study protocol will be eligible to receive open label supplies of VIAGRA™ for 48 weeks or until the time that VIAGRA™ becomes commercially available, whichever comes first.

**Progress:** This study has not yet started.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/051	<b>Status:</b> On-going
<b>Title:</b> Immunohistochemical Localization of Insulin-Like Growth Factor (IGF) Binding Proteins in Prostate Cancer		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> Jan 95	
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC		
<b>Associate Investigators:</b> MAJ Richard R. Gomez, MC CPT Patrick A. Twomey, MC		Stephen R. Plymate, M.D. CPT Michael D. Bagg, MC
<b>Key Words:</b> cancer:prostate, IGF		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: The purpose of this study is to localize IGFBP's -2,-3,-4, and -6 in regions of histologically proven prostate cancer. Additionally, these same techniques will be used to identify these binding proteins in areas of prostatic intraepithelial neoplasia (PIN) and benign prostatic hyperplasia (BPH). The information gleaned from this study will help better understand IGFBP expression in both malignant, premalignant, and benign prostatic tissue.

Technical Approach: Radical prostatectomy specimens will be obtained by the Urology Service and taken to Pathology for histologic sectioning. Prostate adenocarcinoma will be identified in sections (as well as areas of PIN or BPH) with an adjacent section taken for immunohistochemical staining. Immunohistochemical staining will be performed for identification of IGFBP's -4, -2, -3, and -6 in regions of associated neoplasm, PIN or BPH. Approximately 10 patients will be studied with comparisons to be made between neoplastic premalignant, and benign prostatic tissue.

Progress: 40 subjects have been entered in FY 97, for a total of 140 subjects.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 97/039		<b>Status:</b> On-going	
<b>Title:</b> A Multicenter, Phase II, Placebo-Controlled Pilot Study of SNX-111 Administered Intrathecally to Patients with Acute Postoperative Pain					
<b>Start Date:</b> 12/19/96			<b>Est. Completion Date:</b> Aug 97		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> CPT Michael J. Decker, MC			CPT John T. Steedman, MC		
<b>Key Words:</b> Pain, postoperative, SNX-111, placebo					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

Study Objective: The objective of this pilot study is to assess the safety and effectiveness of SNX-111 administered intrathecally to patients with acute, post-operative pain.

Technical Approach: This is a Phase II, multicenter randomized, double-blind, placebo-controlled pilot study to assess the safety and effectiveness of SNX-111 in patients with acute, post-operative pain. All patients will have intrathecal catheters in place for surgical anesthesia. Patients in each of the operative populations will be randomly assigned to receive a placebo, 0.7 µg/hr SNX-111 or 7.0 µg/hr SNX-111 for 48-72 hours. Infusions will begin intraoperatively, after the administration of the intrathecal anesthesia, and continue post-operatively. Drug will be delivered via an external pump and a temporary intrathecal screening catheter. Patients will have a physical exam, labs, ECT and a mini-mental status exam at baseline. During the study, routine pain assessments will be performed every 4 hours while awake and every 8-10 hours during sleep time for the 48-72 hour treatment period. Systemic morphine administered by PCA for pain post surgery. At discharge patients will again have labs and a neuro exam and will return at 2 weeks to assess for adverse events.

Progress: 8 subjects have been entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/144		<b>Status:</b> Completed	
<b>Title:</b> Evaluation of the Safety and Efficacy of Transurethral Resection of the Prostate Using the Contact Laser System vs Electrosurgery					
<b>Start Date:</b> 09/02/94			<b>Est. Completion Date:</b>		
<b>Department:</b> Surgery/Urology			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> LTC Kurt L. Hansberry, MC			COL John N. Wettlaufer, MC		
<b>Key Words:</b> prostate:resection, laser, electrosurgery					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 9/30/97	

Study Objective: 1. To evaluate the effectiveness (resection and coagulation) of the Contact Laser System in comparison to that of electrosurgery for transurethral resection of the prostate (TURP). 2. To evaluate the relative cost effectiveness of the Contract Laser in comparison to that of electrosurgery for transurethral resection of the prostate.

Technical Approach: Male patients who have been diagnosed with symptomatic benign prostatic hypertrophy (BPH) will be enrolled into this study once all of the entrance criteria have been fulfilled. After all baseline evaluations have been performed, each patient will undergo TURP using either electrosurgery or the Contact Laser System. All patients will be monitored closely through discharge, and will undergo follow-up evaluation a one and six months, and one year following surgery. Follow-up evaluation will be encouraged (optional) annually for five (5) years thereafter.

Progress: Twenty patients were entered in this study at MAMC. Contact laser ablation appears to be equally safe and effective when compared to transurethral resection, but superior in shortening catheter time and hospital stay.

**DETAIL SHEETS FOR PROTOCOLS**

**DEPARTMENT OF SURGERY  
VASCULAR SURGERY**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 96/163		<b>Status:</b> On-going	
<b>Title:</b> Clinical Evaluation of the Handling and Performance of the HEMASHIELD Knitted Double Velour Fabric and Polytetrafluoroethylene (PTFE) Patched for Carotid Endarterectomy Patch Procedures in Patients					
<b>Start Date:</b> 09/20/96			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> Surgery/Vascular			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> COL Charles A. Andersen, MC					
<b>Associate Investigators:</b> LTC Stephen B. Olsen, MC CPT Donald M. Collins, MC			LTC David F. J. Tollefson, MC Edmund Kanar		
<b>Key Words:</b> Carotid endarterectomy, HEMASHIELD					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 9/30/97

**Study Objective:** The objective of this randomized, parallel group, multi-center study is to evaluate the performance of the test product, the HEMASHIELD® Knitted Double Velour patch in comparison to the control product, the Gore-Tex patch, for use as a carotid artery patch following carotid endarterectomy in patients.

**Technical Approach:** This is a prospectively randomized, multi-center clinical trial in which a maximum of 40 patients will be enrolled, with approximately equal numbers of patients in each of the 2 treatment groups, Hemashield patch vs. the Gore-Tex patch. Anticipated MAMC enrollment is approximately 20 patients. Patients included in this study will be evaluated preoperatively, intraoperatively, at discharge from the hospital, and at 3 months, 6 months, 12 months and up to a total of 24 months postoperatively. Follow-up evaluations will include a medical history and physical exam at 3, 6, 12 and 24 months and duplex ultrasound testing at 6 and 12 months (with optional duplex scan at 24 months) for assessment of patch repair. Completion of follow-up assessment and final report is anticipated about one and one half years after the first patient enrollment.

**Progress:** 14 subjects were entered during FY 97. 4 were subsequently dropped because 1 subject's surgeon wanted to use the hemashield (study called for use of the Gore-tex patch); 1 subject did not have surgery because of a hypotensive episode; 1 subject's Gore-Tex patch was explanted; and 1 subject had a prolene suture instead of the Gore-Tex suture.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 95/097		<b>Status:</b> On-going	
<b>Title:</b> Abdominal Aortic Aneurysm (AAA) and Chronic Obstructive Pulmonary Disease (COPD); Is There a Relationship					
<b>Start Date:</b> 04/21/95			<b>Est. Completion Date:</b> Mar 96		
<b>Department:</b> Surgery/Vascular			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC David F. J. Tollefson, MC					
<b>Associate Investigators:</b>		CPT Peter J. Armstrong, MC			
LTC William H. Cragun, MC		COL Charles A. Andersen, MC			
LTC Thomas A. Dillard, MC		LTC Stephen B. Olsen, MC			
<b>Key Words:</b> Aneurysm:abdominal aortic, COPD					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		9/30/97	

Study Objective: To determine the association, if any, of AAA and COPD as well as potential pathophysiologic explanation

Technical Approach: A comparison will be made between patients with and without COPD and the incidence of AAA. Patients 50 years and older will be selected from those followed in the pulmonary, family practice or adult primary care clinics who have been determined to have COPD by screening history, spirometry and carbon monoxide diffusing capacity (DLCO). Controls will be age/sex matched without COPD. Selected participants will be evaluated by pulmonary function tests (spirometry, DLCO), serum alpha 1 anti-trypsin levels, serum elastase levels, serum cholesterol levels, ankle-brachial indices and abdominal aortic duplex. The incidence in the control and study groups will be compared through Chi-squared analysis and individual variables will be determined through student T-test. A  $p < 0.05$  will be determined to be statistically significant. Patients and primary care physicians will be notified of the presence or absence of AAA, abnormal ankle-brachial indices, COPD, or hypercholesterolemia.

Progress: 15 subjects have been entered in FY 97.

# DETAIL SHEETS FOR PROTOCOLS

## SOCIAL WORK SERVICE

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/100	<b>Status:</b> On-going
<b>Title:</b> Comparison and Prediction of Completers and Non-completers of A Domestic Violence Program		
<b>Start Date:</b> 06/20/97	<b>Est. Completion Date:</b> Oct 98	
<b>Department:</b> Social Work Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> George T. Mitchell		
<b>Associate Investigators:</b>	April Gerlock Ph.C., ARNP	
<b>Key Words:</b> Domestic violence program, completers, predictors		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** 1) To compare program completers and non-completers on the study variables; and 2) to determine if program completion and non-completion can be predicted.

**Technical Approach:** The following data will be collected, from the male batterer, during the initial interview: demographics; health consequences of domestic violence (DV); early exposure to violence (CTS); substance abuse history (MAST & DAST); legal history; level of battering behaviors (ABI); attitudes about relationship mutuality (MDPQ); physiological/affective response to stress (SOS); self-esteem (SERS); post-traumatic stress (PTSD) threshold (PCL); and court-ordered/probationary status. Certain data will also be collected from the victim/partner, as well, during the initial contact and includes: patterns of his violence (ABI); health consequences of domestic violence; and attitudes about relationship mutuality (MDPQ). Men who have completed the intensive rehabilitation phase and who have moved to the once-a-month maintenance phase will be considered the rehabilitation completers. Non-completers consists of those who either choose to remove themselves from the program or those who are removed because of non-compliance with rehabilitation. Those men who leave the program because of deployment or relocation are dropped from the study because the potential outcome is unknown due to external circumstances. Statistical analyses will include a comparison of the completers and non-completers on the study variables. In addition, the study variables that reveal the greatest difference between completers and noncompleters based on the one-way ANOVA will be entered into a multiple regression analysis to determine which ones account for the greatest variance. A discriminant function analysis will be conducted to determine which variables are best able to predict completion vs. non-completion of DV rehabilitation. Where appropriate, comparison between the reports of the batterers and their victim/partners will be investigated for consistency.

**Progress:** 54 subjects were entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 97/061	<b>Status:</b> Completed
<b>Title:</b> An Assessment of the Characteristics of Spouse Abuse in A Military Population		
<b>Start Date:</b> 03/21/97	<b>Est. Completion Date:</b> Jan 99	
<b>Department:</b> Social Work Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Nancy K. Raiha, MS		
<b>Associate Investigators:</b> COL Robert A. Mays, MC Sheliga V Tamayo F		Browne M Norwood A MAJ Gary D. Southwell, MC
<b>Key Words:</b> Spouse abuse, military population		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

Study Objective: 1) To describe the epidemiological characteristics of spouse abuse in the U.S. Army; 2) to examine the role personality traits and Axis I and Axis II diagnoses may play in contributing to spouse abuse.

Technical Approach: This study will look at approximately 100 military couples (who have been identified as substantiated abuse cases by the Family Advocacy Case Management Team) in an attempt to elucidate aspects of personality and Axis I and Axis II diagnoses. Participants will complete several questionnaires that ask about their own personality and their perception of their partner's personality as well as a questionnaire that measures pathology. Participation in this study will require approximately 2 hours.

Progress: For all medical centers, eight additional subjects were entered in this study in FY 97 for a total of 138 subjects. Two subjects were tested at MAMC. All data have been sent to the central facility for analysis.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 96/139	<b>Status:</b> Completed
<b>Title:</b> Spouse Abuse Among Active Duty Women Married to Civilian Husbands: An Examination of Interpersonal and Social Factors		
<b>Start Date:</b> 08/16/96	<b>Est. Completion Date:</b> Aug 98	
<b>Department:</b> Social Work Service	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Nancy K. Raiha, MS		
<b>Associate Investigators:</b> COL Robert A. Mays, MC Patricia J. O'Campo, Ph.D.		
MAJ Charles D. Magruder, MC MAJ Gary D. Southwell, MC Andrea C. Gielen		
<b>Key Words:</b> Abuse:spousal, active duty women, civilian husbands		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	9/30/97

**Study Objective:** (1) To elucidate possible risk factors for domestic violence in the U.S. Army population. (2) To collect information which would facilitate development of more effective spouse abuse prevention programs in the U.S. Army population. (3) To identify military-unique stressors or circumstances which may contribute to the development of an abusive relationship among Active Duty women. (3) To determine if there is a higher prevalence of certain interpersonal relationship patterns among active duty women and civilian men in an abusive situation.

**Technical Approach:** This study will examine approximately 300 couples who have been identified as substantiated abuse cases by the Family Advocacy Case Management Team. Participants will complete several questionnaires that ask about their life history, current feelings, and how they would describe the relationship between them and their partner. Initial analyses will involve the use of paired-sample t-tests to examine the relationship between husbands and wives on the FES, LISRES, DAS and NEO PI-R's. A chi-square test will be used to examine differences between husbands and wives on the data from the questionnaire. Chi-square Interaction Detector will be used to compare abusive versus control couples. To assess for differences in interrelationships patterns, MANOVA will be used. Canonical correlation will be included in the MANOVA to examine the interrelationship between sets of instrument scores. Once this is accomplished, logistic regression will be done to calculate log-odds ratios of abuse, and nonlinear canonical correlations will be used to examine the relationships between the continuous and categorical sets of variables. Generalized estimating equations will be used as an additional test to assess for the impact of correlation within clusters.

**Progress:** Six additional patients were entered in this multicenter study for a total of 106 subjects. Fourteen couples were tested at MAMC. All data have been sent to the central facility for analysis.

**DETAIL SHEETS FOR PROTOCOLS**

**GYNECOLOGY ONCOLOGY GROUP**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 82/073		<b>Status:</b> On-going	
<b>Title:</b> GOG 0026A: Master Protocol for Phase II Drug Studies in Treatment of Advanced Recurrent Pelvic Malignancies					
<b>Start Date:</b> 11/20/81			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> malignancy:pelvic					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/16/96

**Study Objective:** To implement a master protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment.

**Technical Approach:** A "rejection" type design will be used with a fixed sample size of 25 eligible patients/disease site/drug or combination studied. The design allows replacement of ineffective regimens by newer agents or combinations. Sections relating to specific agents will be sequentially incorporated into this protocol as these agents are studied. Continuing review will be done for each separate protocol. To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy and a granulocyte count  $>1500/\text{mm}^3$ , platelet count  $>100,000/\text{mm}^3$ , BUN  $<25 \text{ mg\%}$ , creatinine  $<1.5 \text{ mg\%}$ , bilirubin  $<1.1 \text{ mg}$ , SGOT  $<5 \text{ IU}$ . Patients receiving myelosuppressive agents will have adequate bone marrow function as described above. Exception to the general requirement for normal liver function will be secondary to documented metastatic tumor to the liver or as noted in the section dealing with that particular agent. Patients with all primary disease sites of gynecologic malignancies are eligible. Each disease site will be accumulated as a separate study sample. For a particular drug study, the allowable disease site(s) may be further qualified. Ascites and pleural effusion alone are not considered measurable for purposes of the study. A steady rise in the titers of alpha-fetoprotein and beta-HCG will be taken as evidence of disease progression in germ cell tumors of the ovary.

**Progress:** No new patients entered in FY 96. One patient remains on protocol in this series (26LL).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 82/007		<b>Status:</b> On-going
<b>Title:</b> GOG 0026C: A Phase II Trial of Cis-Platinum Diamminedichloride in Treatment of Advanced Pelvic Malignancies				
<b>Start Date:</b> 11/20/81		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:pelvic,cisplatinum				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/16/96

Study Objective: To determine the efficacy of cis-platinum diamminedichloride in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer, who have failed higher priority therapies, will be offered cis-platinum as a Phase II drug to determine its efficacy. The drug is given at 50 mg/m<sup>2</sup> intravenously every three weeks as toxicity permits. Patients who respond or who demonstrate disease will continue to receive the agent until progression has occurred.

Progress: No patients have been entered in this study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/008		<b>Status:</b> On-going	
<b>Title:</b> GOG 0026II: Trial of 5-Fluorouracil and High Dose Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b> Ind x		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> pelvic malignancy,5-Fluorouracil,leucovorin:high dose					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
			\$8000.00		02/16/96

**Study Objective:** To implement a protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment. In this case, the agents are 5-FU and high dose Leucovorin.

**Technical Approach:** Patients who have received prior 5-FU are ineligible. Leucovorin will be administered in a dose of 200 mg/m<sup>2</sup> daily for 5 days and repeated at four and eight weeks and thereafter every five weeks. 5-FU will be administered in a dose of 370 mg/m<sup>2</sup>/day for 5 days, infused immediately after the Leucovorin has been given. An adequate trial will be defined as receiving one course of treatment and living four weeks for additional tumor assessment, provided death is not due to tumor progression. All patients entered on the study will be evaluated for toxicity. Patients will remain on study and continue receiving chemotherapy until disease progression or until toxicity prevents further treatment.

**Progress:** No patients have been entered in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/153		<b>Status:</b> On-going
<b>Title:</b> GOG 0026LL: A Phase II Trial of Prolonged Oral Etoposide (VP-16) in Patients With Advanced Pelvic Malignancies				
<b>Start Date:</b> 08/06/93		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:pelvic, etoposide				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		06/21/96

Study Objective: 1. To determine if low dose oral VP-16 given on a daily basis for 21 days out of the month yields significant clinical response in patients who have previously been treated with platinum containing compounds. 2. To evaluate the relative side effects of such low dose therapy.

Technical Approach: Patients with recurrent pelvic malignancies not amenable to curative therapy are eligible. The treatment regimen will consist of oral VP-16 given at 50 mg/m<sup>2</sup>/d on the 1st to the 24th of the month. This will be cycled every four weeks until disease progression or adverse effects prohibit further therapy. Patients will be followed by clinical examinations or if applicable chest x-rays prior to the initiation of each cycle.

Progress: This study was mistakenly terminated in FY 95. It has since been re-reviewed and reactivated. Two patients were entered in FY 94; one is deceased and one is still being followed. The protocol was closed to patient entry, 1 Dec 95.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 81/035	<b>Status:</b> On-going
<b>Title:</b> GOG 0041: Surgical Staging of Ovarian Carcinoma		
<b>Start Date:</b> 01/16/81	<b>Est. Completion Date:</b>	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC                      COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,surgical staging		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	02/16/96

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a completed and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This study was closed to patient entry 12 Feb 87. Thirteen patients were enrolled, 1 has been lost to follow up, 3 have died, 3 are being followed at WRAMC, and 6 are being followed at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 81/105		<b>Status:</b> On-going	
<b>Title:</b> GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma					
<b>Start Date:</b> 08/21/81			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL Roger B. Lee, MC			COL William L. Benson, MC LTC Gordon O. Downey, MC		
<b>Key Words:</b> Cancer:ovarian, adenocarcinoma, cyclophosphamide, Adriamycin, Platinol					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/16/96

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG #25.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This study was closed to patient entry, 20 Jul 85. Six patients were entered in the study and one is still being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 84/033		<b>Status:</b> On-going	
<b>Title:</b> GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease					
<b>Start Date:</b> 02/17/84			<b>Est. Completion Date:</b> Dec 88		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> tumor:ovarian,melphalan,cisplatin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/16/96	

**Study Objective:** To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

**Technical Approach:** Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

**Progress:** This study was closed to patient entry 25 Feb 92. Ten patients were enrolled; 1 has died and 9 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 84/074		<b>Status:</b> On-going
<b>Title:</b> GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the ...				
<b>Start Date:</b> 08/17/84		<b>Est. Completion Date:</b> Jul 89		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,teratoma,tumor:sinus,chemo,bleomycin,cisplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/16/96

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** Closed to patient entry 10 Feb 92. One patient was enrolled in FY 92 and is still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 86/089		<b>Status:</b> On-going	
<b>Title:</b> GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and...					
<b>Start Date:</b> 08/15/86			<b>Est. Completion Date:</b> Feb 94		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL Roger B. Lee, MC			COL William L. Benson, MC LTC Gordon O. Downey, MC		
<b>Key Words:</b> Cancer:cervical, carcinoma, hydroxyurea, 5-FU, Cisplatin, Radiotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/16/96

**Study Objective:** To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

**Technical Approach:** Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

**Progress:** This protocol was closed to patient entry in December 1990 because it was reported that the two patients entered on the study had died (at a different institution). After further review it was discovered that this was a mistake and the protocol was reopened in Feb 93. These two patients are still being followed at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 87/013	<b>Status:</b> On-going
<b>Title:</b> GOG 0090: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors		
<b>Start Date:</b> 10/17/86	<b>Est. Completion Date:</b> Indef.	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC
<b>Key Words:</b> tumor:germ cell:ovary,cisplatin,etoposide,bleomycin,VAC,vincristine,dactinomycin,cyclophosphamide,BEP		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	02/16/96

Study Objective: To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

Technical Approach: After adequate recovery from surgery (if done) previously untreated patients will be treated by three courses of BEP followed by three courses of VAC. Patients exhibiting disease progression on either phase will be taken off study. Patients who had previous VAC or similar regimens will be treated with four courses of BEP. After recovery from BEP therapy, reassessment laparotomy will be performed in patients with negative markers who are clinically free of disease. Progressing patients will be removed from the study. Patients with no evidence of disease at second look will be followed. Patients with persistent disease at second look will be removed from the study. An adequate trial is defined as receiving two courses of the drug and living at least six weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression of disease.

Progress: No patients have been enrolled in this study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/104		<b>Status:</b> On-going	
<b>Title:</b> GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy					
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC COL Donald H. Kull, MC		
<b>Key Words:</b> cancer:cervix,hysterectomy,lymphadenectomy,radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0		<b>OMA Cost:</b> \$0.00		02/16/96	

Study Objective: To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

Technical Approach: All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

Progress: Study was closed to patient entry on 18 Sep 1995. One patient was enrolled in FY 88 and is still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 89/036		<b>Status:</b> Completed	
<b>Title:</b> GOG 0093: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)					
<b>Start Date:</b> 03/17/89			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:ovarian,chromic phosphate,laparotomy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$2416.00
			<b>Periodic Review:</b>		02/16/96

**Study Objective:** To evaluate the role of intraperitoneal chromic phosphate (32P) suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy and to evaluate disease free survival, sites and frequency of relapse, and the morbidity from intraperitoneal 32P therapy.

**Technical Approach:** Patients with primary histologically confirmed epithelial carcinoma of the ovary who are in complete clinical remission, with no persistent or recurrent cancer, and initial FIGO Stage III will be eligible. Patients with distant metastatic disease, previous pelvic or abdominal radiation therapy, previous or concomitant malignancies other than of skin (excluding melanoma), and borderline malignancy of the ovary will be ineligible. Patients will be randomized to one or two regimens. Regimen I will consist of 15 millicuries of intraperitoneal chromic phosphate suspension therapy, preferably within 10 days (but no more than six weeks) after second-look laparotomy. Patients will be randomized before second-look laparotomy and a dialysis catheter will be inserted during second-look laparotomy in those patients randomized to receive 32P. Patients will be rotated every 10 minutes (left side to back to right side) for two hours to facilitate distribution of the 32P. Anterior and lateral scans of the abdominal cavity will be done to evaluate adequate distribution in the peritoneal cavity of the 32P and to confirm that loculation has not occurred. Data collection will continue until disease progression or death.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/028		<b>Status:</b> On-going	
<b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III					
<b>Start Date:</b> 11/21/86			<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> COL William L. Benson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian,cyclophosphamide,cisplatin,P32					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/16/96	

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This protocol was closed to patient entry 14 Mar 94. Five patients have been entered and 1 remains in follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/091		<b>Status:</b> On-going
<b>Title:</b> GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma				
<b>Start Date:</b> 06/19/87		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> COL William L. Benson, MC		COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:endometrial,radiotherapy				
<b>Accumulative</b> <b>MEDCASE Cost:</b>		<b>Est. Accumulative</b> <b>OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		06/21/96

Study Objective: To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

Technical Approach: Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

Progress: Closed to patient entry on 3 July 1995. One patient was enrolled at MAMC during FY 95 and two patients were enrolled in previous years. All are being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 89/052		<b>Status:</b> On-going
<b>Title:</b> GOG 0108: Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC #113891) with or without Cisplatin (NSC #119875) in Patients with Advanced or Recurrent Mixed Mesodermal Tumors of the Uterus				
<b>Start Date:</b> 04/21/89		<b>Est. Completion Date:</b> Indef.		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> tumor:uterus,ifosfamide,cisplatin,uroprotector mesna				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		06/21/96

**Study Objective:** To determine: whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response; the duration of progression-free interval; and the length of survival as compared to doxorubicin alone.

**Technical Approach:** Patients will be randomized to either Regimen I or Regimen II. Regimen I: doxorubicin 60 mg/m<sup>2</sup> IV every three weeks to a maximum total dose of no greater than 500 mg/m<sup>2</sup>. Regimen II: doxorubicin 60 mg/m<sup>2</sup> IV every three weeks plus cisplatin, 50 mg/m<sup>2</sup> IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m<sup>2</sup>. Each regimen will require both dose escalation and dose reduction in accordance with adverse effects observed on the previous course of therapy. Patients who reach maximum doxorubicin dose will undergo a complete re-evaluation. All therapy will then be stopped and the patient followed on no further therapy until progression of disease is documented. Further therapy at that point will be at the discretion of the investigator. Patients on no further treatment will be followed every three months for the first two years, then every six months for three years, and annually thereafter.

**Progress:** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/086		<b>Status:</b> On-going
<b>Title:</b> GOG 0109 (SWOG 8797): A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy, versus Radiation Therapy Alone in Selected Patients with Stages ...				
<b>Start Date:</b> 08/02/91		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:cervix,5-Fluorouracil,cisplatin,radiotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** To determine whether the combination of 5-fluorouracil (5-FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins following radical hysterectomy and lymph node dissection for Stages I-A2, I-B, and II-A carcinoma of the cervix and to determine the increase in toxicities due to 5-FU and cisplatin as an adjunct to radiation therapy versus radiation therapy alone.

**Technical Approach:** Patients must have primary, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix, clinical stages I-A2, I-B, or II-A and must have had a radical hysterectomy with total pelvic lymphadenectomy and para-aortic sampling. Patients must have, at surgical evaluation, either histologically confirmed positive pelvic lymph nodes, positive parametrial involvement, or positive surgical margins. Patients with confirmed positive para-aortic lymph nodes are not eligible. Patients must not have received prior chemotherapy, immunotherapy (including biologics), hormonal therapy, or pelvic irradiation. Patients will be randomly assigned to receive either 5-FU and cisplatin plus pelvic irradiation or pelvic irradiation alone. Patients with positive high common iliac lymph nodes will receive extended field para-aortic irradiation. Irradiation and chemotherapy will begin simultaneously within six weeks after surgery. Chemotherapy will be given once a week every three weeks for four cycles. Radiation therapy will be given for six weeks. After completion of therapy, patients will be followed every 3 months for two years and every 6 months thereafter. Formal analysis of progression-free and overall survival will be performed at 2 1/2 years after the start of patient accrual to determine if consideration should be given to early termination of either treatment arm.

**Progress:** This study was closed to patient entry 20 May 94. No patients were enrolled at MAMC during FY 97. The one patient enrolled previously is still in follow-up.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/064		<b>Status:</b> Terminated	
<b>Title:</b> GOG 0113: An Evaluation of Hydroxyurea, 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative .....					
<b>Start Date:</b> 05/03/91			<b>Est. Completion Date:</b>		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:cervix,hydroxyurea,5-Fluorouracil,cisplatin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/16/96	

**Study Objective:** To evaluate the toxicity and feasibility of infusion 5-FU, cisplatin, and hydroxyurea, given concurrent with pelvic radiation therapy in patients with locally advanced cancer of the uterine cervix.

**Technical Approach:** Multiple studies have confirmed that the presence of metastases to para-aortic lymph nodes is a prognostic factor of greater significance than FIGO Stage. In addition, the pattern of failure in this group is vastly different, with one-half of the recurrences being outside the treated field. Because a major objective of this study is to evaluate local control and survival, this study will be open only to those patients with documented negative para-aortic nodes. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes. Radiation therapy will be given by external beam therapy followed by intracavitary therapy. Cisplatin will be given IV on days 1 and 29 of external radiation therapy; 5-FU will be given IV on days 2, 3, 4, 5, 30, 31, 32, and 33 of external radiation therapy; and hydroxyurea will be given PO four days each week during external radiation therapy. After therapy, patients will be followed every three months for two years and then every six months for three years for progression free interval and survival.

**Progress:** Two patients were enrolled in FY 92 and are still alive. The protocol was terminated by GOG because further data was not needed for the protocol.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/074		<b>Status:</b> On-going
<b>Title:</b> GOG 0115: Bleomycin (NSC #125066), Etoposide (NSC #141540) and Cisplatin (NSC #119875) (BEP) as First-Line Therapy of Malignant Tumors of the Ovarian Stroma (Granulosa Cell, Sertoli-Leydig Tumor, ...				
<b>Start Date:</b> 07/12/91		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> tumor:ovarian stroma,chemo,bleomycin,etoposide,cisplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/16/96

**Study Objective:** To assess the efficacy of bleomycin, etoposide (VP-16), and cisplatin (BEP) chemotherapy in patients with malignant tumors of the ovarian stroma as a first-line regimen.

**Technical Approach:** Eligible patients will be those with histologically confirmed primary Stages II, III, or IV with incompletely resected disease, recurrent or persistent tumor of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord stromal tumor, or sex cord tumor with annular tubules). Patients will undergo, where appropriate, a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Omentectomy, cytologic washings, and other surgical staging such as pelvic and peri-aortic node sampling, multiple pelvic and diaphragmatic node biopsies are optional. Within 8 weeks of surgery, patients will be placed on BEP therapy: bleomycin IV push weekly for nine weeks, etoposide IV daily times five every three weeks for four courses, cisplatin IV daily times five, every three weeks for four courses. Complete responders or patients with nonmeasurable disease will undergo reassessment laparotomy not later than eight weeks following final course of therapy. To be evaluable for response, a patient will receive at least one course of chemotherapy. The efficacy of the three-drug combination will be evaluated by frequency of negative second-look and frequency and severity of acute toxicity.

**Progress:** One patient was enrolled in this study in FY 95 and one patient was enrolled in FY 84. One is still being followed and the other was lost to follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/013		<b>Status:</b> Completed
<b>Title:</b> GOG 0116: Evaluation of Adjuvant VP-16 and Carboplatin Therapy in Totally Resected Ovarian Dysgerminoma				
<b>Start Date:</b> 10/01/93			<b>Est. Completion Date:</b> Apr 96	
<b>Department:</b> GOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovarian, VP-16, carboplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/16/96

Study Objective: To evaluate the efficacy and toxicity of adjuvant VP-16 and carboplatin in patients with totally resected ovarian dysgerminoma.

Technical Approach: Patients who have had totally resected Stage Ib-III ovarian dysgerminoma will be eligible for this study. Those patients will undergo chemotherapy utilizing VP-16 10 mg/m<sup>2</sup> on days 1-3 carboplatin 400 mg/m<sup>2</sup> on day 1. After completion of the chemotherapy, patients will be evaluated in follow-up every two months for one year, every three months for the second year, then every four to six months thereafter for a total of five years. At the completion of the five year follow-up annual evaluations will then be performed. At the time of each follow-up, physical examination, liver function tests, and tumor markers of Beta-HCG and Alpha-fetoprotein will be obtained.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/061		<b>Status:</b> On-going
<b>Title:</b> GOG 0120: A Randomized Comparison of Hydroxyurea vs Hydroxyurea, 5-FU Infusion and Bolus Cisplatin vs Weekly Cisplatin as Adjunct to Radiation Therapy in Patients with Stages IIB, III, IVA Carcinoma..				
<b>Start Date:</b> 03/05/93		<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:cervix, hydroxyurea 5-FU, cisplatin, radiation therapy				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	02/16/96

**Study Objective:** 1) To compare the relative efficacy of radiation sensitization of hydroxyurea alone or in combination with 5-Fluorouracil and Cisplatin versus Cisplatin alone in the treatment of Stages II-B through IV-A carcinoma of the cervix. 2) To determine the relative toxicities of these three different radiation sensitization schemes.

**Technical Approach:** Patients with locally advanced carcinoma of the cervix who have histologically confirmed negative para-aortic lymph nodes will be eligible for this study. Patients who consent will be randomized to three different treatment regimens. All treatment regimens will include the same radiation therapy technique given as standard therapy. Randomization will be between 1) Cisplatin 40 mg/m<sup>2</sup> IV q week X 6, (2) Cisplatin 50 mg/m<sup>2</sup> IV on days 1 & 29 with continuous infusion of 5-FU 1000 mg/m<sup>2</sup> on days 2 - 5 and 30 - 33 and hydroxyurea PO 2 mg/m<sup>2</sup> Mon/Thurs every week during radiation therapy (3) hydroxyurea PO 3 gm/m<sup>2</sup> Mon/Thurs every week during radiation therapy. Following therapy, patients will be monitored every 3 months for first 2 years and then every 6 months for the next 3 years.

To determine the efficacy of cisplatin, the principle parameters to be collected, analyzed and reported are: a) outcome variables (recurrence-free interval and survival) b) tumor characteristics c) host characteristics d) adverse effects (frequency and severity e) therapy administered.

Interim analyses will be conducted at approximately the 2nd, 3rd, 4th and 5th years using a global log-rank test. The goal will be to identify large differences in the recurrence free interval among the three treatment regimens. The interim log-rank test will be adjusted for important prognostic factors.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/014		<b>Status:</b> On-going
<b>Title:</b> GOG 0122: Whole Abdominal Radiotherapy Versus Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma				
<b>Start Date:</b> 10/01/93		<b>Est. Completion Date:</b> Jan 97		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:endometrial, radiotherapy, doxorubicin, cisplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** 1) To compare the effectiveness of chemotherapy to whole abdominal radiation therapy in patients with advanced endometrial cancer which has been resected to less than 2 cm residual tumor. 2) To compare the relative toxicity of these two treatment strategies.

**Technical Approach:** Patients who have had surgical intervention for advanced (Stage III or IV) endometrial carcinoma confined to the abdominal cavity will be randomized either to whole abdominal radiation therapy or chemotherapy utilizing Doxorubicin at 60 mg/m<sup>2</sup> and Cisplatin at 50 mg/m<sup>2</sup> given every three weeks for eight cycles. After the completion of therapy patients will be seen and evaluated every three months for two years and six months thereafter for five years after treatment. Nationally 240 patients will be enrolled over 4 years. Patients will be evaluated for length of survival, disease-free survival and toxicity.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/063		<b>Status:</b> On-going
<b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix				
<b>Start Date:</b> 03/05/93		<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:cervix, radiation therapy, cisplatin, hysterectomy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

**Technical Approach:** This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m<sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens.

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered

**Progress:** One patient was enrolled in this study at MAMC in FY 96, and is in the follow-up phase.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/064		<b>Status:</b> Suspended
<b>Title:</b> GOG 0126C: A Phase II Evaluation of Altretamine (Hexamethylmelamine) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer				
<b>Start Date:</b> 01/20/95		<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovary, altretamine				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** To evaluate the use of altretamine as second-line chemotherapy in patients resistant to platinum containing compounds and taxol.

**Technical Approach:** Patients with epithelial ovarian cancer refractory to platinum containing compounds and taxol will be eligible for participation in this study. Participants in this study will be treated with altretamine at a dose of 260 mg/m<sup>2</sup> daily for 14 days. Treatment cycles will be repeated at 28 day intervals, providing serious side effects or tumor progression do not interfere. During the course of therapy weekly CBC's and liver function tests will be obtained. Should disease progression or severe side effects occur, therapy will be discontinued. Patients will be continued to be followed for life.

**Progress:** This protocol was suspended by GOG in August 1996 until data could be analyzed to determine if enough patients have been accrued. No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/066		<b>Status:</b> Suspended
<b>Title:</b> GOG 0126D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer				
<b>Start Date:</b> 02/16/96		<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovarian, plastinum resistnat, refractory, pyrazoloacridine				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	9/30/97

Study Objective: To evaluate the safety and efficacy of Pyrazoloacridine in the treatment of platinum-resistant and refractory epithelial ovarian carcinoma.

Technical Approach: Patients with recurrent epithelial ovarian cancer who are resistant to platinum containing compounds will be eligible for this study. Subjects will be treated with Pyrazoloacridine, administered intravenously over three hours. Treatment cycles will be repeated every three weeks.

During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each course of treatment a history and physical examination will be performed and routine liver function test will be obtained. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination, however, if measured by CT, ultrasound or chest x-ray it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. If complete tumor resolution occurs treatment will continue at least three cycles, but may continue indefinitely at the discretion of the patient and investigator. Patients who develop febrile neutropenia or a granulocyte count less than 500 will have dose reductions as outlined in the protocol. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays may be supported with Granulocyte-Colony Stimulating Factor (G-CSF). Patients entered into this protocol will be followed for life.

Progress: This protocol was suspended in Feb 96 until data could be analyzed to determine if more subjects were needed. No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/115		<b>Status:</b> Completed	
<b>Title:</b> GOG 0126E: Evaluation of Paclitaxel and SDZ PSC 833 (IND #41232) in Recurrent, Platinum Resistant and Refractory Ovarian Cancer					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, platinum resistant, refractory, paclitaxel, SDZ PSC 833					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To evaluate the safety and efficacy of combined therapy with paclitaxel and the experimental drug SDZ PSC 833.

**Technical Approach:** This study will assess the relative effectiveness of SDZ PSC 833 in overcoming drug resistance to paclitaxel in patients with advanced ovarian cancer recalcitrant to standard chemotherapy. Patients with measurable, histologically proven recurrent ovarian cancer are eligible for this study. Participants in this study will be treated with SDZ PSC 833 at 5 mg/kg orally 3 times a day for 12 doses. Doses will be given no closer than 5 hours apart on consecutive days beginning day one of each cycle. Cycles will be repeated every three weeks. On day two, patients will receive paclitaxel at 70 mg/m<sup>2</sup> intravenously over a three hour infusion time. Patients will be treated until disease progression or adverse effect prohibit further therapy. During the course of therapy routine laboratory and radiologic investigations will be obtained.

**Progress:** This study was closed to patient entry, 30 Jul 97. No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/072		<b>Status:</b> On-going	
<b>Title:</b> GOG 0126G: Evaluation of CI-958 in Recurrent, Platinum Resistant, and Refractory Ovarian Cancer					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, CI-958, platinum resistant, refractory					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		/ /

Study Objective: 1) To estimate the antitumor activity of CI-958 in patients with recurrent or refractory ovarian cancer who have failed on higher priority treatment protocols. 2) To determine the nature and degree of toxicity of CI-958 in this cohort of patients.

Technical Approach: Patients with histologically determined recurrent platinum-resistant epithelial ovarian cancer who agree to participate in this study will be treated with a two hour infusion of CI-958 administered at 21 day intervals. All patients require the placement of a central venous access device because of significant phlebitis resulting from the administration of CI-958. Treatment will continue until the disease progression or unexceptable side effects develop or two cycles pasted a clinical complete response. Initial treatment modification are listed page 11 and 12 of the treatment protocol. Standard hematologic support with granulocyte colony stimulating factor may be utilized at the discretion of the investigator. While on therapy, patients will be evaluated by physical examination and tumor measurements prior to every cycle if the tumor measurements are obtained by physical examination. For those patients requiring radiographic assessment to determine response, tumor measurements will be obtained after every second cycle. All patients will undergo pretreatment assessment by history, physical examination, tumor measurements, CBC with differential and platelets, serum electrolytes, bun, creatinine, Ca, Mg, Phosphate, urinalysis, bilirubin, SOOT, Alkaline Phosphatase, chest x-ray, EKG, CA-125, and Muga Scan. The Muga scan will be repeated after six cycles and then every three thereafter or more frequently if dictated by the patients clinical condition. The patients will be followed subsequent to treatment until death.

Progress: No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/073		<b>Status:</b> On-going	
<b>Title:</b> GOG 0126-H: Evaluation of 24-Hour Continuous Infusion Topotecan in Recurrent, Platinum-Resistant and Refractory Ovarian Cancer					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, topotecan, platinum, refractory					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		/ /

Study Objective: To evaluate the efficacy of 24 Hour continuous infusion topotecan in the treatment of patients with recurrent epithelial ovarian cancer.

Technical Approach: This study will evaluate the safety and efficacy of a 24Hour continuous infusion of intravenous topotecan in patients with histologically documented recurrent epithelial ovarian cancer who have been determined to be platinum-resistant. Platinum-resistance is determined by lack of response to platinum based chemotherapy or recurrence within six months of completion of platinum based chemotherapy. Topotecan will be administered by a 24-hour continuous intravenous infusion at three week intervals. In the event of significant hematologic toxicity, a dose reduction will be accomplished. Hematologic toxicity will be evaluated with weekly CBC's. Prior to patients will be treated at three week intervals. Prior to each treatment cycle a history and physical examination will be performed and the following laboratory evaluation: PT/PTT, BUN/creatinine, bilirubin, total/direct, SGOT/SGPT, alkaline phosphatase, Na, K, Cl, CO2, P, glucose, and urine analysis. In the event that tumor measurements are obtained by imaging studies such as a CT scan or MRI imaging studies will be performed every six weeks for tumor measurement. Chest x-ray and EKG will be obtained prior to every treatment cycle as clinically indicated. Patients will continue treatment until disease progression for the development of unexceptable side effects.

Progress: No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/171		<b>Status:</b> On-going
<b>Title:</b> GOG 0127H: Evaluation of Prolonged Oral Etoposide (VP-16) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix				
<b>Start Date:</b> 07/21/95		<b>Est. Completion Date:</b> Sep 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, squamous cell, etoposide				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	07/19/96	

Study Objectives: To evaluate the safety and efficacy of prolonged oral VP-16 in the treatment of recurrent or metastatic squamous cell carcinoma of the cervix.

Technical Approach: Patients with historically proven or metastatic squamous cell carcinoma of the cervix will be treated with oral VP-16 for 21 consecutive days out of a 28 day cycle. Treatment will be reviewed on day 29 after a one week break. Patients who have received previous radiation therapy will be started at a lower dose initially. Dose modification with either dose reduction or dose intensification is possible depending on marrow rescue. Clinical management, including physical examination and chest x-ray will be obtained prior to each cycle. If additional imaging studies, such as CT ultrasound or MR are required, tumor measurements will be repeated after every other cycle. Treatment will be discontinued should severe toxicity or tumor progression result. There are no treatment comparisons involved and no known historical controls available. The study design will be primarily based on prior GOG experience in this disease entity. This will insure consistency in evaluation of response. Therapy plans demonstrating activity will later be compared and investigated in ensuing phase III studies.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/091		<b>Status:</b> On-going	
<b>Title:</b> GOG 0127-J: Evaluation of 9-Cis Retinoic Acid (9-CRA, NSC #659772) in Persistent or Recurrent Squamous Cell Carcinoma of the Cervix Previously Treated by Chemotherapy					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:cervix, squamous cell, 9-cis retinoic acid, recurrent					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					//

Study Objective: 1. To estimate the anti tumor activity of 9-Cis Retinoic Acid in patients with persistent or recurrent squamous cell carcinoma of the cervix who have failed previous chemotherapy. 2. To determine the nature and degree of toxicity of 9-Cis Retinoic Acid in this cohort of patients.

Technical Approach: Patients with recurrent squamous cell carcinoma of the cervix who have failed previous chemotherapy are eligible for entry into this study. All eligible patients who consent to therapy will be treated with continuous oral 9-Cis Retinoic Acid until disease progresses or adverse effects prohibit further therapy. If tumor measurements are determined on physical examination, tumor measurements will be part of the physical examination prior to each four week course of chemotherapy. In the event of radiologic determination of tumor measurements other than chest x-ray, imaging studies will be performed every two courses. While undergoing therapy a weekly CBC with differential and platelet count will be obtained. Prior to each course of chemotherapy a creatine, bill rubin, SOOT, alkaline phosphatase, triglycerides, calcium, LDH and urinalysis will be obtained. Treatment modifications based of toxicity are outlined in pages 12-15 of the study protocol. All patients will be followed after treatment until death.

Progress : No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/102		<b>Status:</b> On-going
<b>Title:</b> GOG 0128B: Evaluation of Paclitaxel (Taxol) in Persistent or Recurrent Non-Squamous Cell Carcinoma of the Cervix and Vagina				
<b>Start Date:</b> 05/06/94		<b>Est. Completion Date:</b> May 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, Cancer:vagina, paclitaxel				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** To evaluate efficacy of Paclitaxel (Taxol) in the treatment of patients with persistent or recurrent non-squamous cell carcinoma of the cervix or vagina.

**Technical Approach:** Patients with incurable recurrent or persistent non-squamous cell carcinoma of the cervix and vagina are eligible to participate in this study. All patients will receive a 24 hour infusion of Paclitaxel at 170 mg/m<sup>2</sup> every three weeks. Patients who have received previous radiation therapy to the pelvis will be treated at a dose of 135 mg/m<sup>2</sup> every three weeks. Routine weekly CBCs will be obtained to monitor for significant neutropenia. Should significant neutropenia develop resulting in fever or prolonged neutropenia, dose reduction will occur. If a dose of 110 mg/m<sup>2</sup> still results in significant neutropenia, granulocyte colony stimulating factor (G-CSF) will be used. On subsequent treatment cycles, 5 microgram/kg will be administered subcutaneously starting 24 hours after therapy and continuing until absolute granulocyte count is sufficient. Patients will continue to receive Taxol every three weeks until tumor progression occurs or severe side effects prevent further therapy. Tumor measurements will be obtained prior to every cycle if detectable on physical examination. Measurements determined by x-rays or imaging studies will be obtained every 6 weeks.

**Progress:** This study was closed to enrollment in Dec 94 to review data collection. It was reactivated in May 95. No patients have been enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/029		<b>Status:</b> On-going
<b>Title:</b> GOG 0128D: Evaluation of Tamoxifen in Persistent or Recurrent Non-squamous Cell Carcinoma of the Cervix				
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Jan 98	
<b>Department:</b> GOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:cervix, Tamoxifen, hormonal manipulation, HPV				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	/ /	

Study Objective: 1) To evaluate the efficacy of tamoxifen citrate in the treatment of non-squamous cell carcinoma of the cervix. 2) To evaluate the influence of hormonal manipulation on the expression of Human Papilloma Virus (HPV) viral protein products (E6 & E7).

Technical Approach: This study will assess the relative efficacy of tamoxifen citrate in the treatment of advanced recurrent non-squamous cell carcinoma of the cervix. Patients with histologically proven recurrent non-squamous cell carcinoma of the cervix will be eligible for treatment. All patients entered into this study will have a pre-treatment biopsy specimen submitted for the evaluation of the expression of the E6 & E7 protein of the Human Papilloma Virus. Patients will be treated with tamoxifen citrate at 10 mg orally bid. Treatment will continue until there is evidence of disease progression or adverse effects prohibit further therapy. Upon withdrawal of tamoxifen therapy, a further tissue sample will be obtained to re-evaluate the HPV E6 & E7 protein expression. Physical examination, routine CBC will be obtained prior to initiation of therapy and monthly thereafter. Tumor measurements will be obtained on a monthly basis.

Progress : No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/068		<b>Status:</b> On-going	
<b>Title:</b> GOG 0129E: Evaluation of Dactinomycin (Cosmegen) in the Treatment of Recurrent or Persistent Endometrial Carcinoma					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Feb 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:endometrial, dactinomycin					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** To determine if the Dactinomycin has significant activity with an acceptable level of toxicity in patients with advanced or recurrent endometrial carcinoma who have failed standard therapy.

**Technical Approach:** This study will assess the relative efficacy as well as toxicity of intravenous Dactinomycin in patients with histologically documented recurrent or advanced endometrial carcinoma with clinically measurable disease who have failed standard therapy and are not curable by surgery or radiation therapy. Dactinomycin will be given intravenously over 15 minutes every four weeks. Treatment will continue until disease progression or significant toxicity precludes further therapy. In the absence of severe toxicity or tumor progression, the patient may remain on therapy indefinitely at the discretion of the investigator.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/027		<b>Status:</b> Completed
<b>Title:</b> GOG 0130B, Evaluation of Paclitaxel (Taxol) in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus.				
<b>Start Date:</b> 11/18/94		<b>Est. Completion Date:</b> JAN 96		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Mesodermal Tumors of the Uterus				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	/ /	

Study Objectives: To evaluate the efficacy of taxol in the treatment of mixed mesodermal tumors of the uterus.

Technical Approach: Patients with recurrent mixed mesodermal tumors of the uterus who have failed previous therapy are eligible to participate in this study. All patients entered in this study must have clinically or radiologically measurable tumors. Patients will be treated with a 24 hour infusion of paclitaxel at 170 mg/m<sup>2</sup> intravenously. This therapy will be repeated every three weeks until the tumor progresses, side effects intervene, or the patient elects to withdraw from therapy. If the tumor is measurable by physical examination, tumor measurements will be obtained prior to each course of chemotherapy. If, however, radiological investigations are required for determining tumor size, imaging will be performed every 6 weeks. All patients will be treated until disease progression or severe side effects limit subsequent therapy. Annual accrual of approximately 15 patients is expected and approximately 40 are needed for the study.

Progress: This study was closed to patient entry, 13 Jan 97. No patients were enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/074		<b>Status:</b> On-going	
<b>Title:</b> GOG 0130-C: Evaluation of Trimetrexate in the Treatment of Persistent or Recurrent Mixed Mesodermal Tumors of the Uterus					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:uterus, mixed mesodermal, recurrent, trimetrexate					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) To estimate the objective response rate of trimetrexate in patients with advanced, persistent, or recurrent mixed mesodermal tumors of the uterus who have failed standard therapy. 2) To determine the nature and degree of toxicity of trimetrexate in this cohort of patients.

**Technical Approach:** Patients with advanced or recurrent mixed mesodermal tumors of the uterus who have failed higher GOG priority treatment protocols will be eligible for this study. Eligible patients will be treated with oral trimetrexate twice a day for five days every fourteen days until disease progression or unexceptable toxicity develops. Leucovorin support will be administered for grade IV toxicity. Prior to the study patients will have a physical examination and undergo tumor measurements by either physical examination or imaging studies. Laboratory including CBC with differential and platelets, creatine, alkaline phosphatase, SOOT, bilirubin, and serum albumin will be obtained at it's baseline. While on therapy a weekly CBC with platelets and differential will be obtained. Tumor measurements by physical examination or imaging will be repeated every four weeks. Serum bilirubin, albumin, creatine, SOOT, alkaline phosphatase will also be repeated at four week intervals. Subsequent to the completion of treatment, patients will be followed until their death.

**Progress :** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/062		<b>Status:</b> On-going
<b>Title:</b> GOG 0131B: Evaluation of Prolonged Oral Etoposide (VP-16) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus				
<b>Start Date:</b> 02/04/94		<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:uterus, leiomyosarcoma, etoposide				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
				<b>Periodic Review:</b> 02/16/96

**Study Objective:** To determine if the utilization of semi-continuous low dose oral etoposide has significant activity with an acceptable level of toxicity in patients with advanced or recurrent Leiomyosarcoma of the uterus who have failed standard therapy.

**Technical Approach:** Patients with histologically confirmed recurrent or metastatic leiomyosarcoma that have failed local therapeutic measures and have adequate bone marrow, renal, and hepatic function will be invited to participate in this study. Etoposide (VP-16) will be administered at a dosage of 50 mg/m<sup>2</sup>/day, day 1-21 every 4 weeks. If side effects are not severe, a patient may remain on the study agent indefinitely at the investigator's discretion. Likewise, patients with evidence of progressive disease or those with significant side effects or deterioration of performance status may be removed from study at the investigator's discretion. All patients will be followed until death.

**Progress:** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/075		<b>Status:</b> Suspended
<b>Title:</b> GOG 0131-D: Evaluation of Trimetrexate in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus				
<b>Start Date:</b> 03/21/97		<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:uterus, leiomyosarcoma, recurrent, trimetrexate				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		//

**Study Objective:** 1) To estimate the objective response rate of trimetrexate in patients with advanced, persistent, or recurrent Leiomyosarcomas of the uterus who have failed standard therapy. 2) To determine the nature and degree of toxicity of trimetrexate in this cohort of patients.

**Technical Approach:** Patients with advanced or recurrent Leiomyosarcomas of the uterus who have failed higher GOG priority treatment protocols will be eligible for this study. Eligible patients will be treated with oral trimetrexate twice a day for five days every fourteen days until disease progression or unexceptable toxicity develops. Leucovorin support will be administered for grade IV toxicity. Prior to the study patients will have a physical examination and undergo tumor measurements by either physical examination or imaging studies. Laboratory including CBC with differential and platelets, creatine, alkaline phosphatase, SOOT, bilirubin, and serum albumin will be obtained at it's baseline. While on therapy a weekly CBC with platelets and differential will be obtained. Tumor measurements by physical examination or imaging will be repeated every four weeks. Serum bilirubin, albumin, creatine, SOOT, alkaline phosphatase will also be repeated at four week intervals. Subsequent to the comoletion examination or imaging will be repeated every four weeks. Serum bilirubin, albumin, creatine, SOOT, alkaline phosphatase will also be repeated at four week intervals. Subsequent to the completion of treatment, patients will be followed until their death.

**Progress :** This study has met its first stage accrual goal and was suspended to patient entry, 2 Sep 97. No patients were entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/146		<b>Status:</b> On-going	
<b>Title:</b> GOG 0137: A Randomized Double-Blinded Trial of Estrogen Replacement Therapy versus Placebo in Women with Stage I or II Endometrial Adenocarcinoma					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Jun 04		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> cancer:endometrial, estrogen replacement					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

Study Objective: To determine if the use of estrogen replacement therapy significantly increased the risks of developing recurrence of endometrial cancer after primary treatment.

Technical Approach: Patients entered into this randomized, placebo controlled study will be patients with endometrial cancer without evidence of metastatic disease beyond the uterus or cervix. Some patients may have been simultaneously entered into a protocol randomizing them to receive chemotherapy or no chemotherapy. Other patients will have received treatment with or without radiation as recommended by their primary physician and/or by choice. Patients who are randomized to estrogen replacement therapy will be taking estrogen on a daily basis for the duration of the study. Starting at .625 per day and increasing to a maximum of 1.25 per day as needed for hot flashes for three years. Patient compliance is assets by turning in the empty prescription and a medication log. All patients will receive yearly mammograms because of an increased risk of breast cancer in patients with endometrial cancer and to evaluate the potential confounding risk afforded by estrogen replacement in this group of high risk patients. All other follow-up is in a standard fashion.

Progress : No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/087	<b>Status:</b> On-going
<b>Title:</b> GOG 0139: A Randomized Study of Doxorubicin Plus Cisplatin versus Circadian-Timed Doxorubicin Plus Cisplatin in Patients with Primary Stages III and IV, Recurrent Endometrial Adenocarcinoma		
<b>Start Date:</b> 04/02/93	<b>Est. Completion Date:</b> Mar 96	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> cancer:endometrial, doxorubicin, cisplatin, circadian timed doxorubicin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	06/21/96

Study Objective: 1) To evaluate the potential benefit of the administration of Circadian-timed, chemotherapy versus standard administration of chemotherapy utilizing Doxorubicin and Cisplatin. 2) To evaluate the relative toxicities of these two techniques of administration.

Technical Approach: This study will assess the relative benefit either in improved response rate or decreased toxicity by changing the method of delivery of the chemotherapeutic agents from an arbitrarily administered event to a timed delivery method. Patients will be randomized to receive either standard Doxorubicin/Cisplatin infusions given at a dose of Doxorubicin 60 mg per meter squared, IV Push followed by Cisplatin 60 mg per meter squared over 30 minutes immediately following the Doxorubicin in one treatment regimen as opposed to Doxorubicin at the same dose given IV Push over 30 minutes at 6 a.m. with the Cisplatin at 60 mg per meter squared delivered over 30 minutes at 6 p.m. Both chemotherapeutic regimen would be delivered every 3 weeks for a maximum of eight treatments. Dose reduction would occur initially because of advanced age or previous pelvic radiation therapy. Only patients with advanced or recurrent measurable Adenocarcinoma, Adenoacanthoma, Adenosquamous carcinomas, whose potential for cure by radiation therapy or surgery, alone or in combination is very poor. Prior to each cycle of chemotherapy, patients will be evaluated by history, physical examination, and the usual radiologic test required for monitoring tumor response. The treatment will continue for a maximum of eight treatments or until the tumor progresses.

Progress: No patients have entered this study at MAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/092		<b>Status:</b> On-going	
<b>Title:</b> GOG 0141: Treatment of Patients with Suboptimal (Bulky) Stage IB Carcinoma of the Cervix: A Randomized Comparison of Radical Hysterectomy and Pelvic and Para-aortic Lymphadenectomy with or without....					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Nov 02		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:cervix, hysterectomy, lymphadenectomy, vincristine, cisplatin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	/ /		

**Study Objective:** To evaluate the efficacy of neoadjuvant chemotherapy preceding surgical therapy of bulky stage IB cervical cancers.

**Technical Approach:** This study will assess the value of neoadjuvant chemotherapy utilizing vincristine and cisplatin prior to definitive therapy of stage IB (bulky) cervical cancer by radical hysterectomy, pelvic and para-aortic lymphadenectomy. All patients will be treated with radical hysterectomy, pelvic and para-aortic lymphadenectomy unless histologically documented para-aortic lymph node involvement, parametrial extension, or unresectable pelvic lymph nodes are present. Said involvement must be histologically confirmed. Prior to surgery all patients will be randomized to receive neoadjuvant therapy with vincristine at 1 mg/m<sup>2</sup> IV and cisplatin at 50 mg/m<sup>2</sup> IV administered every ten days for three treatments or no chemotherapy. Patients who randomize to chemotherapy will undergo radical hysterectomy, pelvic and paraaortic lymphadenectomy two to four weeks following completion of chemotherapy, unless progression beyond the cervix occurs during chemotherapy. If progression beyond the cervix occurs during chemotherapy they will be treated with radiation therapy. After radical hysterectomy, pelvic and para-aortic lymphadenectomy patients with surgical margins or positive pelvic lymph nodes will receive radiation to the pelvis post-operatively. Patients who have unsuspected para-aortic metastases will be treated with extended field radiation to the para-aortic lymph nodes.

Subsequent to therapy, all patients will be seen every three months times eight and every six months times six and then yearly thereafter.

Prior to treatment and each course of chemotherapy all patients will undergo a physical examination and tumor measurements.

Additionally, tumor measurements will be obtained each week for those patients who require radiation therapy because of extra cervical progression while receiving chemotherapy. Prior to each course of chemotherapy as well as prior to surgery all patients will have a CBC with differential and platelet, creatinine, SGOT alkaline phosphatase, and bilirubin. Patients who receive radiation therapy will have a CBC with differential and platelets obtained weekly during radiation therapy.

**Progress :** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/149		<b>Status:</b> Suspended
<b>Title:</b> GOG 0143: Familial and Reproductive Factors in Ovarian Cancer				
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Aug 95	
<b>Department:</b> GOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:ovarian, familial factors, reproductive factors				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	02/16/96

Study Objective: 1. To further define the epidemiologic pattern of patients with invasive ovarian carcinoma. 2. To store genetic material for comparison should a genetic marker be identified in the future utilizing risk factors for the development of ovarian cancer to target a patient population suitable for screening.

Technical Approach: Patients identified with invasive ovarian carcinoma will be asked to complete a questionnaire. Additionally, two tubes of blood will be obtained and forwarded for storage, for potential DNA analysis. This is an epidemiologic study and requires no follow-up of the patients.

Progress: No patients entered this study at MAMC. Protocol was suspended July 1994, due to meeting first accrual goal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/140		<b>Status:</b> Suspended
<b>Title:</b> GOG 0145: A Randomized Study of Surgery vs Surgery + Vulvar Radiation in the Management of Poor Prognosis Primary Vulvar Cancer and of Radiation vs Radiation & Chemotherapy for Positive Inguinal Node				
<b>Start Date:</b> 08/05/94		<b>Est. Completion Date:</b>		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:vulvar, positive inguinal nodes				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** 1. To determine whether the additional radiation therapy to the area of vulvar resection decreases the risk of recurrent cancer in high risk patients. 2. Whether the addition of chemotherapy along with radiation improves the effect of radiation therapy in decreasing the risk of tumor recurrence in the areas treated by radiation therapy. 3. To evaluate the impact of these therapeutic interventions on the overall quality of life both during and subsequent to treatment. 4. To determine if HPV status alters the risk of local recurrence and/or survival.

**Technical Approach:** Patients with invasive squamous cell carcinoma of the vulva who meet the eligibility criteria will have initial surgery on the vulva and groins. After pathological examination of the specimen, patients will be eligible for randomization to observation or to additional therapy to the vulva. Patients with positive nodes will be randomized to receive radiation alone or radiation and chemotherapy to the inguinal and pelvic nodes. Patient treated with chemotherapy will receive Cisplatin day one, followed by four days of continuous infusion of 5 FU. In addition, patients will complete quality of life questionnaires prior to receiving radiation or chemotherapy, then at three, six, twelve, eighteen, and twenty-four months. All patients will be followed in the OB-GYN Oncology Clinic subsequent to treatment. Initial frequency of follow-up will be at three month intervals for one year, followed by four month intervals for one additional year and then every six months for an additional three years. The patient's disease status will be correlated with the presence or absence of HPV in the tumor and surrounding tissue.

**Progress:** No patients have been enrolled in this study at MAMC. The study was suspended to patient entry 11 Aug 97 due to inadequate accrual; PI is awaiting further instructions from GOG.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/090		<b>Status:</b> On-going	
<b>Title:</b> GOG 0146C: Evaluation of Topotecan (SKF 104864-A) (NSC#609699) in Recurrent, Platinum, Sensitive Ovarian Cancer					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Dec 95		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, Topotecan, Platinum-Sensitive					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 03/21/97

**Study Objective:** To evaluate the safety and efficacy of Topotecan in the treatment of platinum-sensitive epithelial ovarian carcinoma.

**Technical Approach:** Patients with recurrent epithelial ovarian cancer who have previously responded in a favorable fashion to platinum containing compounds will be eligible for this study. Patients who choose to participate will be treated with Topotecan, administered intravenously over thirty minutes daily for five consecutive days. Treatment cycles will be repeated every three weeks from the first day of chemotherapy. During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each course of treatment a history and physical examination will be preformed and routine liver function test (i.e., PT and PTT) will be obtained. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination or routine chest radiography, however, if measured by CT or ultrasound it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays will be supported with Granulocyte-Colony Stimulating Factor (G-CSF) at 5 mcg/kg/day subcutaneously. G-CSF support will be administered the day after the last dose of Topotecan and continued through day 18 or until hematopoietic recovery. No G-CSF will be administered when the white blood cell count is greater than or equal to 15,000/mcL. Patients entered into this protocol will be followed for life.

**Progress:** This study was closed to patient entry, 16 Feb 96, to review the data. It was reactivated, 21 Apr 96. No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/065		<b>Status:</b> Suspended	
<b>Title:</b> GOG 0146D: Evaluation of Pyrazoloacridine (PZA) (NSC #366140) in Recurrent, Platinum-Sensitive Ovarian Cancer					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Jul 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, platinum-sensitive, pyrazoloacridine					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		/ /

Study Objective: To evaluate the safety and efficacy of Pyrazoloacridine in the treatment of platinum-sensitive epithelial ovarian carcinoma.

Technical Approach: Patients with recurrent epithelial ovarian cancer who have previously responded in a favorable fashion to platinum containing compounds will be eligible for this study. Subjects will be treated with Pyrazoloacridine, administered intravenously over three hours. Treatment cycles will be repeated every three weeks.

During the course of therapy, patients will have weekly CBC's and platelet counts. Prior to each treatment, a history, physical examination and routine liver function test will be performed. Additionally, routine blood chemistries will be obtained. Tumor measurements will be obtained every three weeks if measurable on physical examination, however, if measured by CT, ultrasound or chest x-ray it will be evaluated every six weeks. Patients will continue to receive chemotherapy every three weeks until tumor progression or severe toxicity intervenes. If complete tumor resolution occurs treatment will continue at least three cycles, but may continue indefinitely at the discretion of the patient and investigator. Patients who develop febrile neutropenia or a granulocyte count less than 500 will have dose reductions as outlined in the protocol. Patients who develop febrile neutropenia or develop neutropenia long enough to result in repetitive delays may be supported with Granulocyte-Colony Stimulating Factor (G-CSF). Patients entered into this protocol will be followed for life.

Progress: This study was suspended, 4 Jun 96, to review the data. No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/102		<b>Status:</b> On-going	
<b>Title:</b> GOG 0146E: Evaluation of CI-958 in Recurrent, Platinum-Sensitive Ovarian Cancer					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Feb 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, recurrent, platinum sensitive, CI-958					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	/ /	

Study Objective: To evaluate the safety and efficacy of the investigational drug CI-958 in the treatment of recurrent platinum-sensitive ovarian cancer.

Technical Approach: Patients with measurable recurrent platinum-sensitive ovarian cancer entered into this protocol will receive CI-958 at 560 mg/m<sup>2</sup> over two hours every 21 days until disease progression, or two cycles beyond complete clinical response, or until adverse effects prohibit further therapy. All patients will have placement of a permanent central venous access device prior to initiation of the first dose of chemotherapy. Routine laboratory tests will be obtained.

Progress : No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/104		<b>Status:</b> On-going	
<b>Title:</b> GOG 0146F: Evaluation of 24-Hour Continuous Infusion Topotecan in Recurrent and Platinum-Sensitive, or Metastatic Ovarian Cancer					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, platinum-sensitive, recurrent, metastatic, topotecan					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		/ /

**Study Objective:** To evaluate the efficacy of 24-Hour continuous infusion topotecan in the treatment of patients with recurrent epithelial ovarian cancer.

**Technical Approach:** This study will evaluate the safety and efficacy of a 24-Hour continuous infusion of intravenous topotecan. Patients with histologically documented recurrent epithelial ovarian cancer who have been determined to be platinum-sensitive by a recurrence greater than six months after the initial treatment of platinum containing compounds will be treated with the 24-Hour continuous infusion of intravenous topotecan. In the event of significant hematologic toxicity, a dose reduction will be accomplished.

Hematologic toxicity will be evaluated with weekly CBC's. Prior to patients will be treated at three week intervals. Prior to each treatment cycle a history and physical examination will be performed and the following laboratory evaluation: PT/PTT, BUN/creatinine, bilirubin, total/direct, SGOT/SGPT, alkaline phosphatase, NA, K, CL, CO<sub>2</sub>, P, Glucose, and urine analysis. In the event that tumor measurements are obtained by imaging studies such as a CT scan or MRI imaging studies will be performed every six weeks for tumor measurement. Chest x-ray and EKG will be obtained prior to every treatment cycle as clinically indicated. Patients will continue treatment until disease progression for the development of unexceptable side effects.

**Progress :** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 94/094	<b>Status:</b> On-going
<b>Title:</b> GOG 0148: The Clinical Utility of Soluable TNF/LT Membrane Receptors in the Serum of Patients With All Stages of Primary Epithelial Ovarian Cancer		
<b>Start Date:</b> 04/01/94	<b>Est. Completion Date:</b> May 95	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Cancer:ovarian, membrane receptors, tumor necrosis factor, lymphotoxin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	02/16/96

Study Objective: To evaluate the clinical utility of TNF/LT membrane receptor levels in the serum of patients with epithelial ovarian cancers as both a screening test and marker of therapeutic effect.

Technical Approach: This investigation will follow serum TNF/LT membrane receptors in the serum of patients who are undergoing treatment for primary epithelial ovarian cancer under other GOG protocols. Serum will be obtained prior to the first cycle of chemotherapy and then every other cycle thereafter. After the completion of chemotherapy, serum will be obtained every six months for two additional years. In the event that recurrent disease is suspected, serum will be obtained for investigation. The serum samples will be obtained at the time of routine laboratory studies utilized in the monitoring of ovarian cancer patients. No additional phlebotomy is therefore required.

Progress: No patients have been enrolled at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/061		<b>Status:</b> On-going
<b>Title:</b> GOG 0150: A Phase III Randomized Study of Accelerated Hyperfractionated Whole Abdominal Radiotherapy (AHWAR) vs Combination Ifosfamide-Mesna With Cisplatin ... Carcinosarcoma (CS) of the Uterus				
<b>Start Date:</b> 02/04/94		<b>Est. Completion Date:</b> Feb 00		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:uterine, ifosfamide,mesna, cisplatin, abdominal radiotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/16/96

**Study Objective:** To compare the use of combination Ifosfamide with Mesna and Cisplatin to hyperfractionated whole abdomen radiation therapy with regard to tolerance and efficacy in patients with carcinosarcomas of the uterus.

**Technical Approach:** Patients entering this study will have undergone surgical staging, TAH/BSO, and resection of gross intra-abdominal/pelvic disease. They will then be randomized to receive either radiation therapy (given as a hyperfractionated technique) or chemotherapy (utilizing ifosfamide with mesna and cisplatin). The chemotherapy will be administered over a four day period, at three week intervals. Patients treated with radiation therapy will receive twice a day treatments of 3000 cGy to the whole abdomen with a boost to the pelvis to 5000 cGy. Subsequent to therapy, patients will be seen in the clinic at three month intervals for two years and then six month intervals for the remainder of their follow-up, until completion of their analysis. Routine blood work evaluating renal and hepatic status will be obtained throughout therapy and in post-treatment follow-up.

**Progress:** One patient was enrolled in this study in FY 96. She is in the follow-up phase. No adverse events reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/150		<b>Status:</b> On-going
<b>Title:</b> GOG 0152: A Phase III Randomized Study of Cisplatin & Taxol (Paclitaxel) With Interval Secondary Cytoreduction vs Cisplatin and Paclitaxel in Patients with Suboptimal Stage III & V....ovarian carcinoma				
<b>Start Date:</b> 07/01/94			<b>Est. Completion Date:</b> Mar 96	
<b>Department:</b> GOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovarian, cisplatin paclitaxel, cytoreduction				
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b> \$23500.00	
			<b>Periodic Review:</b> 02/16/96	

Study Objective: To determine the impact of interval cytoreductive surgery on the progression free interval, survival and quality of life of patients with suboptimal debulked Stage III & IV epithelial ovarian cancer.

Technical Approach: All patients will have undergone maximal cytoreductive surgery for their cancer prior to entrance into the study. Subsequently, all patients will receive three treatments at three week intervals of Paclitaxel and Cisplatin by intravenous infusion. After three treatment cycles, patients will be re-evaluated to determine tumor response. Patients with stable disease or tumor response will then be randomized to secondary cytoreductive surgery followed by or three more courses of chemotherapy. Those receiving secondary cytoreductive surgery will receive three more courses of chemotherapy after surgery. Quality of life questionnaire will be completed at intervals during and after therapy.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/028		<b>Status:</b> Completed	
<b>Title:</b> GOG 0154: Human Immunodeficiency Virus (HIV) Testing in Patients with Invasive Cervical Carcinoma.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> JUL 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cervical Carcinoma					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		02/16/96

**Study Objectives:** To determine the frequency of HIV infection in patients with all stages of epithelial cervical carcinoma. To evaluate the impact of HIV infection on the treatment and disease course in patients with cervical carcinoma.

**Technical Approach:** All patients who have invasive epithelial cervical cancers and who are less than 50 years of age will be eligible for participation. A list of total patients offered the protocol will be maintained without identifying factors along with those who agree to participate. Patients who agree will be counseled regarding the risks of HIV infection and will complete a questionnaire regarding additional risk factors. All patients who are HIV positive will continue to be followed in this study. They will be followed at six month intervals for one year, then yearly thereafter for the purposes of this study. A clinical summary form will be submitted at the completion of each visit. The GOG statistical Office will attempt match HIV positive patients with HIV negative patients based on age, tumor grade, stage and other potential confounding factors. Patients in both categories will be followed for disease progression or the development of secondary tumors as well as the occurrence of treatment related toxicity.

**Progress:** No patients have been enrolled at MAMC. This protocol was closed to patient entry, 11 Aug 97 due to inadequate accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/029		<b>Status:</b> Completed	
<b>Title:</b> GOG 0155, Evaluation of Alpha-Interferon and Isotretinoin With or Without Zidovudine (AZT) in the Treatment of HIV-Infected Women with Invasive Cervical Carcinoma.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> NOV 96		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cervical Cancer					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/16/96	

**Study Objectives:** To evaluate the anti-tumor affect and toxicity and toxicity profile of combination isotretinon and alpha-interferon in HIV positive patients with cervical carcinoma.

**Technical Approach:** Patients with Bulky stage I and stages II-IV cervical cancer who are HIV positive are eligible for participation. Upon agreeing to participate, further treatment will be determined by the CD4 count. For patients with CD4 counts less than 500, treatment with daily interferon at 6 million units subcutaneously, daily isotretinoin at 1 mg/kg/d orally, and zidovudine (AZT) 100 mg five times per day orally will be initiated. At the end of a four week course, the patients will be re-evaluated. If significant progression of disease, as defined by greater than a 50% increase in tumor volume or the appearance of new lesions, patients will be discontinued for therapy and undergo standard oncologic therapy directed at their cervical cancer. Patients with CD4 counts greater than or equal to 500 will be treated similarly except they will not receive the zidovudine. Weekly CBC's, biweekly liver function tests and lipid profiles will be obtained. At four week intervals, CD4 counts and creatinine levels will also be obtained. After twelve weeks, patients will be evaluated for subsequent tumor-directed therapy. Patients will be followed at three month intervals for 2 1/2 years, at six month intervals for an additional three years and then every year.

**Progress:** No patients have been enrolled at MAMC. This protocol was closed to patient entry, 11 Aug 97, due to inadequate patient accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/095		<b>Status:</b> On-going
<b>Title:</b> GOG 0156: Randomized Trial of Pelvic Radiation versus Doxorubicin Plus Cisplatin in Stage IB, Stage IC, IIA, and IIB EnDometrial Carcinoma				
<b>Start Date:</b> 04/21/95		<b>Est. Completion Date:</b> Jun 00		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:endometrial, radiation, doxorubicin, cisplatin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objective:** Objective: To compare radiation therapy versus chemotherapy in an adjuvant setting for high risk, early stage endometrial cancer.

**Technical Approach:** Patients with high risk Stage IB, IC, IIA, or IIB endometrial cancer will be randomized to receive either post operative radiation therapy or post operative chemotherapy. Radiation therapy will be given in standard pelvic fields to a total dose of 5040 cGy. Patients who are randomized to receive chemotherapy will receive Doxorubicin and Cisplatin therapy given at a dose of 60 mg/m<sup>2</sup> and 50 mg/m<sup>2</sup> respectively. Chemotherapy will be given at three week intervals for a total of six treatment cycles. While receiving therapy, patients randomized to radiation therapy will have weekly CBCs drawn and patients randomized to chemotherapy will have CBCs, liver function test, and creatine obtained immediately prior to the next cycle of chemotherapy. Subsequent to treatment, all patients will be followed at three to four month intervals for two years. Standard follow-up in the Gyn Oncology Clinic involves six month follow-up thereafter until five years from treatment. However, the protocol requires a less liberal follow-up of yearly evaluations after the two year anniversary date of therapy. Patients will be followed for evidence of progressive disease and survival.

**Progress:** No patients have been enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/096		<b>Status:</b> On-going
<b>Title:</b> GOG 0157: A Randomized Phase III Trial of Carboplatin (AUG 7.5) and Paclitaxel 175 mg/m <sup>2</sup> q 21 Days x 3 Courses versus the Same Regimen x 6 Courses in Patients With Selected Stage IC and II (A,B,C)...				
<b>Start Date:</b> 04/21/95		<b>Est. Completion Date:</b> May 01		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovarian, carboplatin, paclitaxel				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	04/18/97	

**Study Objective:** 1. To evaluate the role of Taxol in the treatment of early stage high risk epithelial ovarian cancers. 2. To determine the optimal number of treatment cycles for the treatment of high risk early stage epithelial ovarian cancer.

**Technical Approach:** Patients entered into this study will be treated with intravenous Carboplatin at an area under the curve of 7.5. Taxol at 175 mg/m<sup>2</sup> will also be administered. Treatments will be provided intravenously at three week intervals. During the course of chemotherapy, weekly CBCs will be obtained to evaluate toxicity. Prior to each treatment cycle, a history and physical examination will be performed as well as creatine, CA-125 and urinalysis. Other investigative tests will be ordered as needed only. Patients will be randomized prior to the initiation of therapy to receive three or six cycles of chemotherapy. Dose reduction or the addition of G-CSF to reduce myelosuppressive side effects are outlined in the protocol. The primary modality to reduce toxicity will be dose reduction followed by the administration of G-CSF for repeated episodes or for febrile neutropenia. After the completion of therapy, patients will be followed in the GYN Oncology clinic on a monthly basis for six months and then every three months for four follow-up visits. Thereafter, they will be followed on a yearly basis for life.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/072		<b>Status:</b> On-going	
<b>Title:</b> GOG 0158: A Phase III Randomized Study of A Platinum Compound and Paclitaxel in Optimal Stage III Epithelial Ovarian Carcinoma: Cisplatin vs Carboplatin and 3-Hour vs 96-Hour Infusions of Paclitaxel					
<b>Start Date:</b> 01/20/95			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovary, cisplatin, carboplatin, paclitaxel, G-CSF					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$56222.00
			<b>Periodic Review:</b>		09/19/97

Study Objective: To compare the relative efficacy and toxicity of two different platinum compounds when utilized with taxol in two different infusions schemes for the treatment of patients with optimally debulked epithelial ovarian cancer.

Technical Approach: Patients with optimally debulked Stage III epithelial ovarian cancer who agree to participate in this study will be randomized to four different treatment regimens. The treatment regimens will have two different variables (platinum compound selected - cisplatin or carboplatin and duration of infusion - 3 hours or 96 hours). All patients will be treated at three week intervals. Treatment will consist of six treatments followed by a second-look (reassessment laparotomy). Patients with progressive disease or obviously elevated CA-125's (> 100) will not be required to undergo a second-look laparotomy. After the completion of reassessment laparotomy, patients will be followed at monthly intervals for six months followed by three month intervals for additional 36 months and then every six months thereafter. Physical examinations and CA-125s will be obtained during follow-up.

Progress: No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/067		<b>Status:</b> Completed	
<b>Title:</b> GOG 0159: A Phase II Study of Goserelin Acetate (Zoladex) in Recurrent or Persistent Endometrial Cancer					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Jul 97		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:endometrial, Zoladex					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	/ /	

**SSStudy Objective:** To evaluate the effectiveness of the gonadotropin releasing hormone analogue Goserelin Acetate in treating patients with recurrent or persistent Endometrial Cancer.

**Technical Approach:** This study will assess the relative effectiveness of monthly Goserelin Acetate in the treatment of patients with recurrent or persistent endometrial cancer. Patients must have measurable disease with two dimensional measurements of at least 1 cm in each direction if measured by physical examination or chest x-ray, or 2 X 2 cm if measured by other radiologic assessments. Base line observation in tests will be obtained prior to therapy. After initiation of Goserelin Acetate at 3.6 mg subcutaneously every four weeks, follow up physical examination and laboratory evaluation will be obtained as outlined in the protocol. Therapy will continue at least two courses unless there is rapidly progressive disease, and for at least 12 courses if there is no change in disease and if tolerable toxicity is present (Grade 1 and 2). Patients who achieve complete remission will continue on therapy indefinitely. All other patients will continue until progression of disease or if the disease is stable at the discretion of the study chairman. Patients who develop thromboembolic disease will be removed from the study.

**Progress:** No patients have entered this study at MAMC. This protocol was closed to patient entry, 2 Dec 96, because it had met its total accrual goal/



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/093		<b>Status:</b> On-going	
<b>Title:</b> GOG 0160: Evaluation of Anti-HER2 Antibody in Recurrent or Refractory Ovarian Cancer					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:ovarian, recurrent, refractory, anti-HER2					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		/ /	

**Study Objective:** To evaluate the safety and efficacy of recombinant anti-HER2 antibody in the treatment of recurrent or refractory ovarian cancer.

**Technical Approach:** Patients with measurable HER2 antigen positive recurrent ovarian cancer will be treated with weekly 90 minutes intravenous infusions of rhuMAb HER2 until disease progression. The initial dose will be delivered at 4mg/kg with subsequent doses at 2mg/kg. Patients will be measured for disease status by standard physical examination or radiologic studies. Weekly laboratory tests will be obtained. Subsequently, patients will be seen every eight weeks or three visits then every twelve weeks until termination of the study.

Patients who respond and subsequently progress are eligible for retreatment at an increased dose level of 4mg/kg weekly.

**Progress :** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/114	<b>Status:</b> On-going
<b>Title:</b> GOG 0162: A Phase III Randomized Trial of Cisplatin with Paclitaxel Administered by Either 24 Hour Infusion or 96 Hour Infusion in Patients with Selected Stage III & Stage IV Epithelial Ovarian Cancer		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> May 01	
<b>Department:</b> GOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC		
<b>Associate Investigators:</b> None		
<b>Key Words:</b> Cancer:ovarian, epithelial, cisplatin, paclitaxel, 24 vs 96 hr infusion		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

Study Objectives: To compare the safety and efficacy of 24-hour infusion versus a 96-hour infusion of paclitaxel in the treatment of advanced ovarian cancer. To correlate pharmacokinetics of paclitaxel with clinical outcome.

Technical Approach: This study will assess the relative safety and efficacy of 24-hour versus 96-hour infusion times for the administration of paclitaxel in the treatment of ovarian cancer. Patients with selected Stage III ovarian cancer who are not eligible for other GOG studies may participate in this study. Patients are randomized to receive either of the two study treatments. The 96-hour infusion may be administered as an inpatient or as an outpatient utilizing a standard chemotherapy pump. All patient will receive the administration of paclitaxel followed by cisplatin. Treatment will be administered at three week intervals form the beginning of the previous cycle for a total of six cycles. Grade IV myelosuppression will be modified by dose reduction. GCSF may be utilized for acute febrile episodes. In the event of persistent Grade IV myelosuppression, patients will be removed from the study. Patients with measurable disease will be followed with CT-scans after every other cycle. All patients will have a pre-chemotherapy CT as well as a CT-scan at the completion of therapy. CA-1125 levels will also be followed at regular intervals. Subsequent to treatment, patients will be followed at three month intervals for at least the first year for study and points as well as standard follow-up for ovarian cancer patients. Correlation between pharmacokinetics and clinical outcomes will be made at the conclusion of the study. All patients will receive four samples for pharmacologic studies.

Progress: No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/030		<b>Status:</b> On-going	
<b>Title:</b> GOG 0163: A Randomized Study of Doxorubicin Plus Cisplatin Versus Doxorubicin Plus 24-Hour Paclitaxel Plus G-CSF in Patients with Primary Stage III & IV or Recurrent Endometrial Carcinoma					
<b>Start Date:</b> 11/15/96			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> GOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:endometrium, doxorubicin, cisplatin, paclitaxel, G-CSF					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		/ /	

**Study Objective:** To compare the efficacy of doxorubicin plus cisplatin versus doxorubicin plus 24-Hour paclitaxel in the treatment of patients with advanced or recurrent endometrial cancer.

**Technical Approach:** Patients eligible for this protocol will be randomized to receive doxorubicin with either cisplatin or paclitaxel with G-CSF support. Treatment will occur at every three week intervals for a total of seven treatments unless disease progression occurs. Dose reduction and/or the administration of G-CSF will be utilized to reduce the impact of myelosuppression. Cardiac toxicity will be monitored with ejection fractions prior to the initiation of therapy and after three and six cycles. The cumulative dose of doxorubicin will be limited to 420 mg/m<sup>2</sup> in regimen I and 350 mg/m<sup>2</sup> in regimen II.

**Progress :** No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/103		<b>Status:</b> On-going
<b>Title:</b> GOG 0164: A Randomized, Controlled Intergroup Trial of Salvage Therapy with Paclitaxel and Carboplatin versus Salvage Therapy with Stem Cell Supported High-Dose Carboplatin, Mitoxantrone, and ....				
<b>Start Date:</b> 05/16/97		<b>Est. Completion Date:</b> Jan 02		
<b>Department:</b> GOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:ovarian, salvage therapy, paclitaxel, carboplatin, mitoxantrone, cyclophosphamide				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		//

Study Objective: To compare the efficacy of standard salvage chemotherapy to high-dose chemotherapy with stem cell support in improving overall survival, disease survival, or improved quality of life.

Technical Approach: This study will assess the relative efficacy of high-dose chemotherapy with autologous bone marrow or stem cell support utilizing carboplatin, mitoxantrone and cyclophosphamide versus a more standard dose intense regimen of paclitaxel and carboplatin. Patients will be evaluated regularly for disease status every three weeks for three months, then every three months from two years from the start of treatment. In addition to physical examination laboratory perimeters and quality of life assessments will be obtained as per the master protocol. Details of the plan of management and baseline eligibility can be obtained from the master protocol.

Patients randomized to standard chemotherapy will be treated as outpatients at Madigan Army Medical Center. Patients randomizing to the high-dose chemotherapy arm with support will be treated at Brook Army Medical Center, an approved SWOG transplant center.

Progress : No patients have been enrolled in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/030		<b>Status:</b> Terminated
<b>Title:</b> GOG 9303, Cisplatin-DNA Adducts in Ovarian Cancer as a Predictor of Response to Platinum-based Chemotherapy.				
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> MAR 96	
<b>Department:</b> GOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Mark E. Potter, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:ovarian, platinum, chemotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/16/96	

**Study Objectives:** To determine if the level of Platinum-DNA adducts predict responsiveness to the chemotherapeutic regimen of Taxol-Cisplatin in advanced ovarian cancer.

**Technical Approach:** This investigation is a companion protocol to GOG 152, which investigates the utilization of interval cytoreduction in patients treated with cisplatin and taxol for bulky advanced ovarian cancer. Only patients who are entered in to protocol GOG 152 are eligible for participation in this protocol. Consequently, there are no additional risks for surgery or chemotherapy from participation in this protocol. Subjects will have 40-50 cc of blood drawn 24 hours after administration of the first dose of cisplatin. No additional blood or tissue samples will be obtained. All information regarding tumor response and patient survival will already be provided and available as per protocol 152. The blood levels of DNA products will be analyzed with regard to the response to chemotherapy and overall patient survival.

**Progress:** No patients have been enrolled at MAMC. This protocol was terminated because sufficient data had been collected.

**DETAIL SHEETS FOR PROTOCOLS**

**NATIONAL SURGICAL ADJUVANT  
BREAST & BOWEL PROJECT**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/147		<b>Status:</b> On-going	
<b>Title:</b> NSABP R-03: A Clinical Trial to Evaluate the Worth of Preoperative Multimodality Therapy (5-FU-LV and RTX) in Patients with Operable Carcinoma of the Rectum					
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> NSABP			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> cancer:rectum, 5-FU, leucovorin, radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	11/17/95	

**Study Objective:** 1). To determine whether the administration of chemotherapy (chemo) with radiotherapy (RTX) preoperatively is more effective than administration of chemo and RTX (C&R) postoperatively in improving disease-free survival and survival in patients with operable carcinoma of the rectum. 2). To determine if the administration of the above C&R preoperatively results in improve-ment local recurrence rates when compared with the regimen administered post-operatively in this population of patients. 3). To evaluate the response of rectal tumors to preoperative C&R and to correlate that response with disease-free survival and survival. 4). To assess the downstaging effect of preoperative C&R on the tumor size and pathologic status of regional lymph nodes. 5). To estimate the proportion of patients who can be converted to sphincter-saving surgical procedures from abdomino-perineal resection and local excision alone.

**Technical Approach:** Patients with operable adenocarcinoma of the rectum will receive seven cycles of 5-FU (FU) + leucovorin (LV) and radiotherapy (RTX), where the first three cycles are given preoperatively and the remaining four postoperatively, to seven cycles of FU-LV and RTX given postoperatively. The patients will be randomized into 2 groups. Group 1 patients, in cycle 1, will receive LV 500 mg/m<sup>2</sup> by IV infusion and FU 500 mg/m<sup>2</sup> will be started 1 hr later. Treatment will be given weekly for 6 weeks followed by a rest period. Treatment will be restarted 21 days after the date of administration of the sixth dose of the previous cycle. RTX will begin after completion of cycle 1. FU 325 mg/m<sup>2</sup>/day and LV 20 mg/m<sup>2</sup>/day will be given for 5 days during the first and fifth weeks of RTX (cycles 2 and 3). Surgery will be performed after completion of radiation therapy. After recovery from surgery, four more cycles of FU with LV, as in cycle 1, will be given for a total of seven cycles. Groups 2 patients should have surgery performed no later than 3 weeks after randomization. Chemo will begin after recovery from surgery is complete but no later than 4 weeks postoperatively. LV and FU will be administered as in Group 1. RTX will begin after completion of cycle 1. Cycle 4 should begin after completion of RTX when counts allow, but no later than 5 weeks. Four more cycles of FU with LV will be given for a total of seven cycles.

**Progress:** No patients have yet been enrolled at MAMC.

**DETAIL SHEETS FOR PROTOCOLS**

**PEDIATRIC ONCOLOGY GROUP**



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/145		<b>Status:</b> On-going	
<b>Title:</b> POG 0942: A Study of Minimally Invasive Surgery of the Chest in Children with Solid Tumors, A Phase III Intergroup Study					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> MAJ Randall M. Holland, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:solid tumors, pediatric, surgery					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		07/18/97	

**Study Objective:** 1) To compare the morbidity and mortality rates of open surgical procedures with that of MIS; 2) to compare MIS with conventional surgery in obtaining adequate pathologic material for diagnostic and special biological studies; 3) to compare MIS with conventional open surgery in the assessment of tumor resectability; 4) to assess the impact of MIS and open surgery on short-term quality of life (QOL). Several domains of QOL will be examined including surgery-related pain, physical, social and emotional functioning, and global ratings of health and overall QOL; 5) to compare post-procedure recovery time of MIS with conventional surgical techniques in children with cancer; 6) to evaluate and compare post-procedure pain in MIS with conventional surgical techniques; 7) to compare MIS with standard open surgical techniques in regards to the economic costs; and 8) to provide pilot data on a new instrument for assessing QOL in a pediatric population.

**Technical Approach:** This study proposes to determine the role of MIS in the management of pediatric cancer. This Phase III randomized study will test whether MIS is as efficacious as standard open surgical operations for the diagnosis and assessment of resectability of pediatric solid tumors, and whether MIS improves recovery and convalescence in addition to decreasing the cost of care for children with cancer. Eligible patients are those who require surgical intervention for diagnosis and staging, evaluation for disease progression or response to therapy, or for supportive or medical management issues during the course of cancer treatment.

**Progress:** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/141		<b>Status:</b> On-going	
<b>Title:</b> POG 8650: Intergroup National Wilms' Tumor Study - 4					
<b>Start Date:</b> 06/09/93			<b>Est. Completion Date:</b> Oct 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> cancer:pediatric, Wilms'					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 04/21/95	

**Study Objective:** To compare 1) the relapse-free and overall survival percentages of patients with: Stage I and II favorable histology (FH) and Stage I anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D; 2) Stages 3 and 4 FH, and Stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy; 3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy; and 4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

**Technical Approach:** All patients will be <16 years of age, have had no prior chemo-radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol. Patients will be randomized as follows: Stage II/FH & Stage I Ana receive A + V (24 wks) or P/I A + V (18 wks), Stage II/FH receive A + V (22 vs 65 wks) or P/I A + V (60 wks), Stages III & IV FH & clear cell (I-IV) receive A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT, and Stages II-IV Ana receive A + V + D + C (65 wks) plus RT or A + V + D + C (65 wks) plus RT. Legend: A = actinomycin D, V = vincristine, D = doxorubicin (Adriamycin), C = cyclophosphamide, and RT = radiation therapy.

**Progress:** This protocol was closed to patient entry, 1 Sep 94. One patient enrolled at MAMC in FY93 is being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/052		<b>Status:</b> On-going	
<b>Title:</b> POG 8930: A Comprehensive Genetic Analysis of Brain Tumors					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Nov 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:brain, genetics					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/21/97

**Study Objective:** 1) To determine prospectively the clinical significance of abnormalities of cellular DNA content, as measured by flow cytometry in pediatric brain tumors. 2) To determine the clinical implications of cytogenetic abnormalities found in pediatric brain tumors at diagnosis. 3) To determine the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively-acting loci in DNA extracted from pediatric brain tumors. 4) To attempt to derive tumor cell lines and to provide a bank of frozen brain tumor tissue for use in further studies, especially molecular genetic studies.

**Technical Approach:** This is a non-therapeutic study intended to prospectively collect tissue from newly diagnosed patients with brain tumors. Flow cytometry, cytogenetics, and molecular studies will be used to characterize abnormalities of the DNA and correlate their findings with type of disease/diagnoses, tumor grade, and prognostic indicators.

**Progress:** No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/018		<b>Status:</b> On-going	
<b>Title:</b> POG 9031: Treatment of Children with High Stage Medulloblastoma: Cisplatin/VP-16 Pre vs Post-Irradiation					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Nov 94		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> cancer:meduloblastoma, cisplatin, VP-16, radiation					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>10/20/95</b>

**Study Objectives:** To compare the 2-year event-free survival (EFS) of children with newly-diagnosed high-risk medulloblastoma who are treated with cisplatin and VP-16 pre-irradiation vs post-irradiation. To define the toxicity and activity of pre-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. To determine whether achievement of a measurable tumor response (PR and CR) to pre-irradiation cisplatin/VP-16 has prognostic significance for children with high-risk medulloblastoma, compared with failure to achieve a measurable response (SD or PD). To define the toxicity and activity of post-irradiation cisplatin/VP-16 in patients with newly-diagnosed high-risk medulloblastoma. To determine if c-myc amplification in medulloblastoma is associated with an adverse prognosis.

**Technical Approach:** Studies in children and adults have demonstrated the ability to deliver pre-radiotherapy chemotherapy for patients with newly-diagnosed brain tumors without increasing neurotoxicity in association with the subsequent radiotherapy. This approach creates a phase II "window" allowing evaluation of response in these patients who are previously untreated except for surgery. The theoretical anti-neoplastic advantage of this approach is the potentially enhanced efficacy of the radiotherapy when given to "chemically debulked" patients. Half of the children diagnosed with medulloblastoma are now being successfully treated and are surviving for prolonged periods. Until recently, the survival of this group of patients was limited so that long-term effects of therapy were not a concern. As survival increases, one would expect to observe an increase in frequency of certain treatment-related toxicities. There are now a variety of long-term effects which need to be considered in this cohort of patients. Specific evaluations will be made on all patients entered onto this study, so that treatment-related problems may be detected in their early stages and intervention taken. This approach should ultimately improve the quality of life for children diagnosed and treated for brain tumors.

**Progress:** This protocol was closed to patient entry 26 March 96. One patient was enrolled in this study at MAMC in FY95 and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/164		<b>Status:</b> On-going	
<b>Title:</b> POG 9047: Neuroblastoma Biology Protocol					
<b>Start Date:</b> 09/03/93			<b>Est. Completion Date:</b> Feb 96		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>			COL Stephen R. Stephenson, MC		
LTC Shirley E. Reddoch, MC			COL Bruce A. Cook, MC		
LTC Kelly J. Faucette, MC					
<b>Key Words:</b> cancer:neuroblastoma, biology					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		04/18/97
			\$0.00		

**Study Objective:** 1) To obtain tissue for the analysis of DNA content of neuroblastoma cells by flow cytometry. 2) To characterize neuroblastoma tumor DNA from POG patients genetically by analysis of N-myc amplification and LOH for chromosome 1p. 3) To develop a reference bank of genetically characterized tumor tissue and DNA that would be available for other studies.

**Technical Approach:** This is a non-therapeutic study intended to collect tissue from newly-diagnosed neuroblastoma patients  $\leq 21$  years. Viable tumor tissue, frozen tumor tissue (or marrow) and serum will be collected and forwarded to a designated study site.

**Progress:** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/008		<b>Status:</b> On-going	
<b>Title:</b> POG 9153: Intergroup Rhabdomyosarcoma Study/Laboratory Evaluation of Tumor Tissue					
<b>Start Date:</b> 11/04/94			<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Rhabdomyosarcoma					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/21/97

**Study Objective:** 1) To prospectively correlate clinical features and outcome of newly diagnosed children with rhabdomyosarcoma with cytogenetic abnormalities of their tumors, 2) to measure cellular DNA content by flow cytometry of tumor cells and correlate the DNA index of tumor stem lines with clinical features and treatment response, 3) to determine prospectively the clinical significance of amplification or rearrangement of specific cellular proto-oncogenes or allelic loss of recessively acting loci in DNA extrated from pediatric rhamdomyosarcomas, 4) to attempt to derive tumor cell lines and to provide a bank of frozen rhabdomyosarcoma tumor tissue for use in further studies, especially molecular genetic studies, and 5) to determine the degree of specificity of monoclonal antibody probes, 4.2A8, 5.1H11, and 3.1G11, for childhood rhabdomyosarcoma.

**Technical Approach:** This is a non-therapeutic study intended to collect tissue from newly-diagnosed rhabdomyosarcoma and undifferentiated sarcoma patients  $\leq 21$  years. Viable tumor tissue, frozen tumor tissue and involved marrow samples will be collected and forwarded to a designated study site.

**Progress:** One patient enrolled in this study at MAMC in FY 96 and continues to be followed. No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/084		<b>Status:</b> On-going
<b>Title:</b> POG 9182: HIV/Malignancy Biology Protocol				
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Apr 97	
<b>Department:</b> POG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC				
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC	
<b>Key Words:</b> Cancer:lymphoma, HIV				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
			<b>Periodic Review:</b> 02/21/97	

**Study Objective:** 1) To establish a national registry of pediatric AIDS-associated lymphomas and other malignancies and a repository of well-characterized tumor tissue, cells and sera from affected patients. 2) To conduct prospective Phase I-III clinical trials of anti-cancer and anti-retroviral therapies aimed at improving outcomes and identifying critical determinants of risk. 3) To identify the presence and quantify the viral burden of human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), Human Herpes virus 6 (HHV6), and Herpes Simplex virus (HSV) in the tumor tissue, peripheral blood cells, plasma, and cerebrospinal fluid of pediatric patients with lymphomas and other malignancies; and to characterize the effect of anti-cancer and antiviral chemotherapy with regard to lymphoma stage, disease progression, host response, and toxicity. 4) To conduct the first large-scale molecular epidemiologic study of risk factors related to development of HIV-related NHL in children by means of a case-control analysis of HIV-infection characteristics such as co-infection with EBV, CMV, HHV6, Mycoplasma, the quantitative host viral burden, level of immunodeficiency, and other host characteristics. 5) For HIV+ and HIV- children, to characterize differences in NHL tumor tissue in terms of immuno-phenotype, immunoglobulin gene rearrangements and oncogene (c-myc) activation.

**Technical Approach:** Three groups of children are eligible for this protocol. The first, a "case" group, consists of children with a newly-diagnosed malignancy who are HIV positive. The second, a "malignancy control" group, consists of children with a newly-diagnosed malignancy who do NOT have HIV infection. The third group, a "non-malignancy control" group, consists of children with no evidence of malignancy, but who have a documented HIV infection. A total of 150, 150, and 300 patients, respectively is expected. The subject will be seen in the clinic at least every two months for up to two years, then every 6 months up to 3 years. At each visit blood will be drawn for testing. In addition, a small piece of tumor tissue or other body fluids (including spinal fluid and bone marrow), already obtained as part of routine clinical management may be examined. We will establish a database as a repository for characteristics of pediatric patients with HIV infection and malignancies. The database will include all appropriate clinical parameters, laboratory measures, and results of molecular and virologic studies. Descriptive analyses of clinical and laboratory data will use various criteria to characterize the study population and to correlate variation in infectious virus and total viral burden with clinical course and other laboratory measurements. Primary endpoints, which may include tumor response, disease-free survival and episodes of grade 3-4 toxicities, will be confined to those specified in POG therapeutic protocols. Contingency tables relating the laboratory variables with stage, age, primary tumor site, histopathology, and clinical response will be produced. Conditional logistic regression will be used to compare biological data for cases to matched controls. Frequency matching will be performed at the Statistics Office at the time of analysis. Kaplan-Meier life tables, log rank tests, and Cox regression will be used to explore the relationship of laboratory variables to outcome.

**Progress:** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/056		<b>Status:</b> On-going
<b>Title:</b> POG 9201: ALINC #16 Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia, A Pediatric Oncology Group Phase III Study				
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99	
<b>Department:</b> POG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC				
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC	
<b>Key Words:</b> leukemia:pediatric, leukemia:lymphoblastic, cytosine arabinoside, leucovorin calcium, hydrocortisone, 6-Mercaptopurine, methotrexate, E. coli asparaginase, Erwinia aspara				
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>	\$0.00
			<b>Periodic Review:</b> 11/21/97	

**Study Objective:** 1) To confirm the outstanding results in patients with lesser risk not-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (AlinC 14, Arm A). 2) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.

**Technical Approach:** Patients on this study will be treated with a 3-drug induction regimen (vincristine, prednisone, and L-asparaginase) to bring about remission (a state of no apparent disease) in four weeks.

This will be followed by a consolidation phase including (6) six courses of intravenous (into vein) intermediate-dose methotrexate (each will require hospital stay) at 3-week intervals. After week 5, daily 6-mercaptopurine will be given by mouth until the end of planned treatment. Methotrexate will be given intramuscularly (into muscle) weekly. Periodic "pulses" (infrequent administration) of vincristine and prednisone will be given throughout the first two years of therapy. Additionally, triple intrathecal (into spinal fluid) therapy (TIT) consisting of methotrexate, hydrocortisone, cytosine arabinoside will be given at the start of treatment and periodically through the first two years of therapy to prevent the spread of leukemia to the central nervous system (CNS). The vitamin Leucovorin will be given to prevent methotrexate toxicity. After week 25, during the continuation phase, all medications will be on an outpatient basis.

The total duration of therapy is planned to be 2 1/2 years from initial diagnosis. If tests at that time indicate no evidence of leukemia, then all medications will be stopped and you (your child) will be followed closely to be sure that there is no evidence of return of the disease.

**Progress:** One patient enrolled in this study at MAMC in FY 96 and another patient was accepted in transfer. Both continue to be followed. No patients were enrolled in FY 97.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/033		<b>Status:</b> On-going	
<b>Title:</b> POG 9219: Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase IV Study					
<b>Start Date:</b> 11/05/93			<b>Est. Completion Date:</b> Jun 96		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>			COL Stephen R. Stephenson, MC		
LTC Shirley E. Reddoch, MC			COL Bruce A. Cook, MC		
LTC Kelly J. Faucette, MC					
<b>Key Words:</b> Cancer:non-Hodgkin's, cyclophosphamide, adriamycin, prednisone, methotrexate, 6-mercaptopurine, ARA-C, hydrocortisone					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		04/18/97	

**Study Objective:** 1. To maintain a high cure rate with minimum toxicity for children with localized non-Hodgkin's lymphoma in favorable sites. 2. To analyze in a large group of patients with localized non-Hodgkin's lymphoma (by pooling data from POG #83314, #8719 and the current study) prognostic factors which may predict subgroups of patients with a poor prognosis within the subgroup of patients with localized NHL.

**Technical Approach:** After staging, subjects that qualify will receive Vincristine 1.5 mg/m<sup>2</sup> (max 2 mg) IV q wk x 6 weeks, prednisone 40 mg/m<sup>2</sup>/day in 3 divided doses x 28 days, Adriamycin 40 mg/m<sup>2</sup>/day IV days 1 & 22, and Cyclophosphamide 750 mg/m<sup>2</sup>/day IV days 1 & 22. Fluid intake is to be > 3000 ml/m<sup>2</sup> on day of treatment. Triple intrathecal chemotherapy (TIT) will be given on days 1, 8, and 22 to those with head and neck primaries. On day 43, or when blood counts recover, the patient will receive Adriamycin 40 mg/m<sup>2</sup> IV, Cyclophosphamide 750 mg/m<sup>2</sup> IV, Vincristine 1.5 mg/m<sup>2</sup> (max 2 mg) IV, and Prednisone 50 mg/m<sup>2</sup> in 3 divided doses x 5 days. On day 64 and when blood counts have returned to normal following the prescribed induction and consolidation regimen, the patient will be assessed for remission status.

**Progress:** Two patients were enrolled in this study at MAMC in FY 97. Both patients completed treatment and continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/148		<b>Status:</b> On-going
<b>Title:</b> POG 9233/34: A Phase III Randomized Trial of standard vs Dose-Intesntified Chemotherapy for Children Less Than 3 Years of Age With A CNS Malignancy Treated With or Without Radiation Therapy				
<b>Start Date:</b> 08/06/93		<b>Est. Completion Date:</b> Jun 95		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC				
<b>Associate Investigators:</b>		COL Stephen R. Stephenson, MC		
LTC Shirley E. Reddoch, MC		COL Bruce A. Cook, MC		
LTC Kelly J. Faucette, MC				
<b>Key Words:</b> cancer:CNS, pediatric, chemotherapy, radiotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		04/18/97

**Study Objective:** To develop effective methods of treatment for very young children with malignant brain tumors that will minimize late toxicities affecting immature and rapidly developing central nervous systems.

**Technical Approach:** Patients < 3 yrs of age with a primary intracranial malignancy will be randomized to one of two regimens. Patients assigned to Regimen A will receive six 12-week courses of chemotherapy, given over a total of 72 weeks. Each course consist of 3 drug cycles. Cycle A; vincristine and cyclophosphamide and Mesna will be given on weeks 1, 13, 25, 37, 49 and 61. Vincristine will be repeated on day 8 of this cycle. During Cycle B, patients will receive cisplatin on day 1 and VP-16 on days 3 and 4. Patients on Regimen B will receive eight 9-week courses of chemotherapy. Each course will consist of 2 consecutive cycles of one drug combination (Cycle X) followed by a cycle of another combination (Cycle Y). On Cycle X, vincristine, and Mesna will be given on day 1 of weeks 1, 4, 10, 13, 19, 22, 28, 31, 27, 40, 49, 55, 58, 64, and 67. On day 2 patients will receive cyclophosphamide and Mesna. On days 3-15 patients will receive G-CSF. On Days 8 and 15, vincristine will be given. Cycle Y will be given on weeks 7, 16, 25, 34, 43, 52, 61 and 70. On Day 1 of Cycle Y, cisplatin will be given. VP-16 will be given on days 3 and 4. On days 5-14 G-CSF will be administered.

Patients experiencing progression or recurrence of disease at any time during or within 12 months of chemotherapy will be encouraged to begin radiation therapy immediately. If disease recurs later than 12 months after completing chemotherapy, patients will be discontinued from the study.

**Progress:** One patient was enrolled in July 94 , completed treatment and was transferred to WRAMC Aug 96. No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/096		<b>Status:</b> On-going	
<b>Title:</b> POG 9315: A Phase III Study of Large Cell Lymphomas in Children and Adolescents; Compariosn of APO vs. APO + IDMTX/HDARA-C and Continuous vs. Bolus Infusion of Doxorubicin					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:lymphomas, chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 04/18/97

**Study Objective:** 1) To study whether intermediate-dose methotrexate/high dose ARA-C (ID MTX/HRARA-C), administered during the maintenance phase can improve the event-free survival (EFS) of patients with advanced-stage large cell lymphoma (LCL); 2) to further characterize the immunophenotypic and morphologic correlates of pediatric LCL; and 3) to compare efficacy and cardiotoxicity of doxorubicin given by continuous versus bolus infusion.

**Technical Approach:** Patients will be randomized at registration to Regimen A or B. Patients who present with CNS disease will go after induction directly to Regimen B. Induction for both regimens will be the same, with additional intrathecal for patients with CNS disease. Maintenance A consists of 8 cycles of ID MTX/HD Ara-C alternating with 5 cycles of VCR/6-MP/ADR/Pred and 2 cycles of VCR/6-MP/MTX/Pred; a total of 15 cycles given at 3 week intervals. Maintenance B consists of 5 cycles of ADR/V/6-MP/Pred followed by 10 cycles of MTX substitution for ADR; a total of 15 cycles will be given at 3 week intervals. Following completion of therapy, examinations will be every month for the first 6 months; thereafter every 3 months until year 2 off therapy and then every 6 months until 5 years off therapy, then annually. Cardiac exams after completion of therapy will be required during first, third and fifty years off treatment.

**Progress:** One patient was enrolled in this study at MAMC in FY 97; however, she was transferred to a civilian hospital prior to her sponsor's separation from the military. This study remains open for patient accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/072		<b>Status:</b> On-going	
<b>Title:</b> POG 9317: Chemotherapy for Children with Advanced Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B Cell ALL					
<b>Start Date:</b> 03/04/94			<b>Est. Completion Date:</b> May 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:Burkett's lymphoma, ARA-C, cytoxan, Vincristine, Adriamycin, Methotrexate, VP-16, Ifosfamide					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 04/18/97

**Study Objective:** 1) To evaluate the efficacy of adding VP-16/Ifosfamide intensification to the treatment of patients with advanced-stage B-cell malignancies: Stage III & IV DU NHL and B-cell acute lymphoblastic leukemia (B-ALL). 2) To compare the toxicity and efficacy of high-dose Ara-C given by intermittent bolus (q 12 hour x 4) vs bolus/continuous infusion over 48 hours.

**Technical Approach:** In this groupwide protocol, we propose to add, in a randomized study, two agents active in the treatment of aggressive NHL: Ifosfamide 2.8 g/m<sup>2</sup> with VP-16 100 mg/m<sup>2</sup> qd x 5. All patients in this study will be randomized at diagnosis to receive, throughout therapy, high-dose Ara-C by continuous infusion (CI) or by bolus (actually a 3 hour infusion). The CI Ara-C dose is base on the POG pilot study #9190 with a starting dose of 3.8 g/m<sup>2</sup>/48 hours (80 mg/m<sup>2</sup>/hr) following 9.5 g/m<sup>2</sup> bolus. The bolus Ara-C dose is taken from POG #8617: 3 g/m<sup>2</sup> q 12 hr X 4 doses. All patients will receive therapy based on POG #8617/8616, with a reduction in duration. After a common induction with fractionated cyclophosphamide, vincristine, Adriamycin, methotrexate by 24-hour infusion, and Ara-C, patients with Stage III disease will receive these drugs without Adriamycin and patients with Stage IV/B-ALLL will receive these 5 drugs including Adriamycin during consolidation. Patients will also be randomized to receive or not to receive VP-16/ifosfamide intensification, except for patients with CNS involvement who will be assigned to receive VP/16 ifosfamide. The study question is being posed in a randomized 2 X 2 factorial design.

**Progress:** No patients have been enrolled in this study at MAMC in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/168		<b>Status:</b> On-going	
<b>Title:</b> POG 9323: Interferon-Alpha 2b Plus Hydroxyurea and Ara-C for Chronic Phase ACML in Children, A POG Pilot Study					
<b>Start Date:</b> 07/21/95			<b>Est. Completion Date:</b> Jul 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:Leukemia, ACML, inteferon, hydroxyurea, Ara-C					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 06/21/96

**Study Objective:** 1) To assess the toxicity of the combination of Hydroxyurea (HU) and Ara-C combined sequentially with interferon-alpha 2b (IFN) in children with adult type chronic myelogenous leukemia (ACML). 2) To determine the frequency and duration of hematologic and cytogenetic response, and the length of time needed to achieve response during two years of such treatment.

**Technical Approach:** Therapy will be divided into 2 induction phases and a consolidation phase. Induction 1: Therapy will begin with two, or possibly three, weekly courses of hydroxyurea and Ara-C. Each course will consist of treatment given on three consecutive days as follows: after consuming clear fluids only for breakfast, hydroxyurea will be taken by mouth. Two hours later, Ara-C will be administered intravenously over 15 minutes. This will be repeated on the second and third day of each course. Subjects will receive at least two courses, beginning days 1 and 8. If blood counts are still above certain values on day 15, a third course will be given. Induction 2: Once blood counts have adequately recovered from the above chemotherapy, IFN treatment will begin. Subjects will receive IFN given as a subcutaneous injection daily for 14 days. Consolidation: IFN will then be continued at this dosage every Monday, Wednesday and Friday. IFN therapy will be interrupted for at least one week, approximately every 6 weeks, for a threeday course of hydroxyurea/Ara-C. This six-week cycle (IFN three times weekly for five weeks followed by a course of hydroxyurea/Ara-C), will be repeated for a total treatment time of approximately two years, assuming a good response to treatment. Most therapy will be administered at home (IFN) or in the outpatient clinic (hydroxyurea/Ara-C), with the exception being the first course of hydroxyurea/Ara-C and the first few days of IFN therapy, for which hospitalization is recommended. Every effort will be made to continue treatment for at least 90 days. All patients who have signs of progressive (worsening) disease within the first 90 days will be evaluated for possible discontinuation of this therapy. All other patients will continue on treatment for a total of 24 months. For those patients continuing on therapy past 90 days, the treatment will be discontinued (prior to 24 months) if there are signs of progressive disease at any time; if there is no evidence of any improvement by six months or if side effects develop which cannot be tolerated even with reduction in the drug dosages. Therapy may also be stopped at any time if a suitable marrow donor has been found and the physician decides that bone marrow transplantation would be in the patient's best interest. If the patient is still on therapy and responding well after 24 months, then the physician may offer to continue therapy with IFN alone. This will be offered as further therapy, but it will not be part of this study. It is not known how many years interferon may be safely given. The dosage schedule described above is to be considered a guideline. It is very possible that modification will need to be made depending on the side effects encountered.

Routine blood tests will be done during the first four to six weeks of therapy (the "induction" phase), and then every one to two weeks while on therapy. A bone marrow aspirate and biopsy will be done prior to start of induction therapy, then twice more at about three month intervals, and then every six months thereafter unless removed from the study because of no response, progressive disease (increased severity), or bone marrow transplantation. A Chromosomal analysis will be completed on each bone marrow aspirate to find out if the Philadelphia chromosome is present. Each bone marrow aspirate will be followed by an ultrasound study of the spleen in order to determine the size of the spleen.

**Progress:** One patient was enrolled in this study at MAMC in FY95. She was taken off study in July 97 to pursue bone marrow transplant and continues to be followed. No patients were enrolled in FY 97..

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/092		<b>Status:</b> On-going
<b>Title:</b> POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for .....Osteogenic Sarcoma				
<b>Start Date:</b> 04/01/94		<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC				
<b>Associate Investigators:</b> COL Bruce A. Cook, MC		LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:pediatric, cancer:sarcoma, doxorubicin, cisplatin, methotrexate, Ifosfamide, MTP-PE				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	04/19/96	

**Study Objective:** 1) To improve the survival of patients with osteogenic sarcoma. 2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma. 3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide. 4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery. 5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs. 6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma. 7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifoxfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** Two patients were enrolled in this study at MAMC in FY 96. One patient chose to discontinue treatment early. The other patient completed therapy. Both patients continue to be followed. No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/086		<b>Status:</b> On-going	
<b>Title:</b> POG 9354: A Randomized Phase III Evaluation of Intensified Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide in the Treatment of Newly-Diagnosed Ewing's Sarcoma or Primitive ...					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone, Cancer:soft tissue; vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/21/97

**Study Objective:** 1) To compare the event-free survival (EFS) and survival of newly diagnosed patients with Ewing's sarcoma and primitive neuroectodermal tumor (PNET) of bone or soft tissue receiving a 48 week standard regimen of vincristine, cyclophosphamide and doxorubicin alternating with ifosfamide and etoposide with G-CSF to those receiving a 30 week dose intensified regimen of the same chemotherapeutic agents. 2) To assess the diagnostic value and prognostic significance of histologic subtype as defined by routine histology, immunochemistry, electron microscopy, and MIC-2 gene expression. 3) To estimate the frequency of occurrence of serious toxicities and adverse orthopedic outcomes associated with the disease and therapy employed, and to compare them between the regimens. 4) To estimate the occurrence of second malignant tumors in these patients. 5) To determine if event free survival and survival differs between patients with PNET and Ewing's sarcoma, and between PNE and Ewing's sarcoma of bone compared to PNET and Ewing's sarcoma of soft tissue.

**Technical Approach:** Subjects will be assigned to one of the two regimens. Regimen A will use drugs according to the standard treatment for Ewing's Sarcoma. Regimen B will utilize the same drugs, in higher doses, over a shorter time period. It is not clear at the present time which of the treatment regimens is better. Whether randomized to Regimen A or Regimen B, the drugs listed below will be given as follows: Vincristine will be given IV push (into vein, quickly). Cyclophosphamide will be given by IV infusion over 30 minutes, (Regimen A); or 6 hours (Regimen B). MESNA will be given to prevent bleeding from the bladder which can be caused by ifosfamide or cyclophosphamide. It will be given intravenous infusion simultaneously with the cyclophosphamide or ifosfamide and will continue to be infused for 3 hours following the end of the cyclophosphamide or ifosfamide dose. Three additional doses of MESNA will be administered by IV over 15 minutes at 3, 6 and 9 hours following the end of the cyclophosphamide dose. Doxorubicin will be given by continuous infusion over 2 days. G-CSF will be given subcutaneous (SC, into the skin) or IV over 2 hours. Etoposide (VP-16) will be given IV over 1 hour. Ifosfamide will be given IV over 1-3 hours.

**Progress:** One patient was accepted in transfer from WRAMC in FY 96 and continues to be followed. One patient was enrolled in this study at MAMC in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/087		<b>Status:</b> On-going	
<b>Title:</b> POG 9362: A Phase II Study of Alpha Interferon in HIV-Related Malignancies					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:all types, HIV, Interferon					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		02/21/97

Study Objective: 1) To Estimate the complete response rate for HIV related malignancies treated with interferon (aIFN). 2) The secondary objectives are to estimate the one year disease free survival and to evaluate the toxicity of aIFN alone or in combination with anti-retroviral therapy.

Technical Approach: This study will require all patients to be enrolled in POG 9182 and compliance with all specimen submission requirements of that protocol. The study will minimize additional tissue, CSF or blood sampling except as required for monitoring for toxicity and tumor response. This study will take advantage of the demonstrated antitumor and antiviral activity of aIFN alone or in combination with other antiretroviral agents to treat HIV positive children with refractory or newly diagnosed malignancies. As the duration of response is one of the goals of this study, responders will continue on therapy indefinitely. Patients on this study will be treated using a interferon by subcutaneous injection every day for 14 days; then if your child's/adolescent's evaluation allows further treatment he/she will receive a interferon three times a week. This treatment will need to be monitored by a treating physician and blood tests will be performed in order to insure that the treatment is well tolerated and that the dose is appropriate. For that purpose 10cc of blood will be taken once a week. The physician and/or staff will be checking closely to see if any of these side effects are occurring. Routine physical exams, laboratory tests and tests such as biopsy or bone marrow aspiration may be necessary to monitor the effect of the treatment. Side effects usually disappear after the treatment is stopped. In the meantime, the doctor may prescribe medication to keep these side effects under control.

Progress: No patients were enrolled in FY 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/088		<b>Status:</b> On-going	
<b>Title:</b> POG 9382: Molecular Studies of t(11;22) Translocation in Ewings' Sarcoma and Peripheral PNET of the Bone					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:Ewing's sarcoma, Cancer:neuroectodermal, Cancer:bone					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) To determine if the presence of minimal metastatic disease as measured by PCR imparts a poor prognosis in patients with localized disease at diagnosis. 2) To determine the prevalence of minimal residual and metastatic disease in the bone marrow and peripheral blood of patients with Ewing's Sarcoma or PPNET as measured by PCR amplification of the t(11;22) chromosomal translocation. 3) To correlate the presence of minimal residual or metastatic disease at diagnosis with other clinical parameters. 4) To determine the types and frequency of chromosomal breakpoints and fusion transcripts and to identify whether certain chromosomal breakpoints correlate with clinical outcome. 5) To determine at what rate patients with clinically documented metastatic disease (at diagnosis or relapse) have evidence of circulating cells with the t(11;22) translocation in peripheral blood, bone marrow, or other body fluids (e.g. CSF, pleural fluid, etc.).

**Technical Approach:** For those subjects who are consented, will have their tumor, blood, and bone marrow looked at for residual disease. An additional blood sample will be obtained just prior to the 2nd course of chemotherapy, and at the completion of the study. Molecular studies will then be performed on these items. Statistical inference will be applied to the primary objective (#1), with descriptive measures being utilized to address the remaining objectives, which are viewed as hypothesis generating. Because of the difficulty in obtaining prior information regarding the PCR measurements, no a prior power calculations can be done. Based on POG 8850, accrual of 45 patients/year could potentially be achieved, for a total of 180 in 4 years. To test whether the presence of minimal metastatic disease as measured by PCR defines a poor risk group, we will conduct three one-sided log-rank tests on event-free survival, using a Bonferroni correction (i.e., each test will use  $\alpha=0.05/3=0.0167$ ). The tests will be done at diagnosis, end of cycle 2, and end of therapy, with the two EFS curves at each time point being defined according to whether the PCR is positive or negative.

**Progress:** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/058		<b>Status:</b> On-going	
<b>Title:</b> POG 9400: ALinC 16 Classification (C) Protocol					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> leukemia:pediatric, laboratory classification					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/21/97

**Study Objective:** 1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission.

2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis.

3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t ( 9; 2 2 ) or t ( 1; 19 ) chromosomal abnormalities. (optional)

4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia.

5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional)

6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional)

7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL.

8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

**Technical Approach:** A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

**Progress:** Two patients enrolled in this study at MAMC in FY95 and one patient enrolled in FY 96. No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/144		<b>Status:</b> On-going	
<b>Title:</b> POG 9404: T-Cell #4 Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced Stage Lymphoblastic Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Aug 04		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Shirley E. Reddoch, MC			LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:lymphoblastic leukemia, T-cell, Cancer:non-Hodgkin's lymphoma					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 07/18/97

**Study Objective:** 1) To determine, in a randomized trial, the effectiveness of high dose methotrexate (HD MTX) when added to a multi-agent chemotherapy backbone (DFCI 87-0001) proven effective in T-Cell acute lymphoblastic leukemias (T-ALL) and advanced stage non-Hodgkin's lymphoma (Lymphoblastic NHL); 2) to determine, in a randomized trial, the role of the cardioprotectant Zinecard (DZR) in preventing cardiotoxicity in children with T-ALL and advanced stage Lymphoblastic NHL receiving an anthracycline based regimen; 3) to study the biology of T-Cell lymphoid malignancies by accumulating data on the concurrent ALL classification study (POG 9400) and analyzing the data relative to outcome; 4) to evaluate the correlation of minimal residual disease with event-free survival utilizing the TAL 1 proto-oncogene; 5) to determine the role of p53 and p16 tumor suppressor genes in T-ALL; and 6) to determine if drug sensitivity profiles of blasts cells to Doxorubicin, methotrexate and cytarabine correlate with initial response and subsequent development of relapse.

**Technical Approach:** Patients will receive induction therapy (weeks 1-6), vincristine every week for 4 weeks, prednisone for 21 days starting day 1 and doxorubicin on days 1, 2, and 22, with or without ZINECARD. During this phase, the drug methotrexate will be given on day 2. Patients will be randomized to receive high dose methotrexate on day 22. Intrathecal methotrexate, Ara-C and hydrocortisone will be given to prevent central nervous system disease throughout the entire three phases of treatment. Once remission has been achieved, patients will receive consolidation therapy (weeks 7-33). Drugs will be given in three week cycles (6-mercaptopurine for 14 days, vincristine and doxorubicin on day 1 of the cycle, prednisone for 21 days) with or without ZINECARD. Asparaginase will also be given during the consolidation phase once a week during weeks 7-26. Patients who received high dose methotrexate on day 22 of induction will also receive it on weeks 7, 10 and 13 of consolidation. At weeks 22-24, all patients will receive radiation therapy to the brain. During continuation (weeks 34-108), patients will receive vincristine, prednisone (every day for five days) and 6-MP (every day x 14 days) every three weeks. Methotrexate, will be given every week except during those weeks when patients receive intrathecal medications.

**Progress:** No patients were enrolled in this study at MAMC in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/059		<b>Status:</b> On-going	
<b>Title:</b> POG 9405: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> leukemia:peds, leukemia:lymphoblastic, Calcium leucovorin, cytosine arabinoside, E. coli L-asparaginase, Erwinia L-asparaginase, hydrocortisone, 6-mercaptopurine, methotrexate					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					11/17/95

**Study Objective:** 1) To determine in a randomized trial, the efficacy of a higher (2.5 gms/mt) versus standard (1 gm/m2) dose methotrexate (MTX) infusion during consolidation. The major endpoint will be eventfree survival among those achieving a complete remission. Secondary comparisons will include sitespecific events and adverse drug reactions. 2) To determine in a randomized comparison, the efficacy of delivering oral 6-MP on a once versus twice daily schedule during continuation. 3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405 and 9406. 4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Approach:** In this research study, the subject will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as Prednisone, given orally (by mouth) for 28 days; vincristine, given by a quick intravenous infusion (IV push) on days 1, 8, 15, and 22; L-asparaginase, injected into a muscle (IM) on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, Icotosine arabinoside (Ara-CI, and hYdrocortisone will be administered intrathecally (injected into the spinal fluid) at various intervals throughout both the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. After Induction the subject will be randomized (assigned by chance, such as flipping a coin), to a specific regimen to include either standard or high dose IV Methotrexate and receiving oral 6MP once or twice daily. During the period of consolidation (weeks 5-28), the subject will receive the drugs methotrexate and 6-mercaptoPurine (6-MP). The Methotrexate will be given at a standard or higher dose. In the first week, methotrexate will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotresate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days. This 2 week treatment will be repeated for a total of 12 cycles. During the period of continuation (weeks 20-130), 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once each week. Patients randomized onto regimens B & D will receive 6MP orally twice daily. The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies. These studies will help the doctor to better understand this form of cancer and how treatment can be improved in the future. Chemotherapy given intrathecally into the spinal fluid may cause pain at infusion site, pain in the back, legs or head, fever, headache, vomiting; rarely stiff neck, convulsions, paralysis. Bone marrow aspiration may cause bruising and soreness over the bone from which the marrow sample is taken.

**Progress:** This protocol closed to patient accrual 2 Dec 95 due to excessive neuro toxicity. One patient enrolled in this study at MAMC in FY95 was taken off study but continues to be followed. Another patient enrolled in FY 96 was transferred to Beaumont Naval Med Ctr.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/060		<b>Status:</b> On-going	
<b>Title:</b> POG 9406: ALinC #16 - Protocol for Patients With Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL)					
<b>Start Date:</b> 12/16/94			<b>Est. Completion Date:</b> Dec 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>			LTC Shirley E. Reddoch, MC		
COL Bruce A. Cook, MC			LTC Kelly J. Faucette, MC		
<b>Key Words:</b> leukemia:pediatric, calcium leucovorin, ARA-C, E. coli asparaginase, Erwinia asparaginase, PEG asparaginase, hydrocortisone, Daunomycin, 6-mercaptopurine, methotrexate					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		11/21/97	
\$0		\$0.00			

**Study Objective:** 1) To determine the efficacy of a 2.5 gm/m<sup>2</sup> dose versus 1 gm/m<sup>2</sup> does intravenous methotrexate infusions during intensified continuation therapy. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events and adverse drug reactions. 2) To determine whether intensified continuation therapy delivering pulses of Ara-C (3 gm/m<sup>2</sup> x 4 doses) with asparaginase rescue is superior to standard intensified continuation with pulses of VM-26/Ara-C. The major endpoint will be event-free survival among those achieving a complete remission. Secondary comparison will include site-specific events (including secondary AML) and adverse drug reactions. 3) To study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406. 4) To assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy.

**Technical Approach:** In this research study, a child will receive intensive combination chemotherapy for 4 weeks to eliminate visible disease (remission induction). This induction chemotherapy involves standard combinations of such agents as prednisone, given orally for 28 days; vincristine, given by a quick intravenous infusion on days 1,8,15, and 22; L-asparaginase, injected IM on days 2, 5, 8, 12, 15, and 19. The drugs methotrexate, cytosine, arabinoside (Ara-c), and hydrocortisone will be administered intrathecally at various intervals throughout the induction and intensive periods to prevent the leukemia from coming back in the central nervous system. Daunomycin will be given on days 8, 15, and 22 intravenously. After the previous treatment, subjects will be randomized to a specific regimen to include either standard or high does Methotrexate or low or high dose Ara-C. During the period known as consolidation, the subject will receive the drugs methotrexate and 6-mercaptopurine (6-MP) during weeks 5-6, 10-11, 15-16, 25-26, and 30-31. In the first week of each of these periods, methotrexate (either the standard or the intensified higher dose) will be injected into a vein followed by a 24-hour infusion. The vitamin Leucovorin will be given orally or as an infusion to help protect the patient from the toxicity of methotrexate. Immediately after the methotrexate, 6-MP will be given by IV infusion over 20 minutes followed by an infusion over 6 hours. On the second week of therapy, the subject will receive methotrexate injected into a muscle (IM) on day 1 and 6-MP daily by mouth for 7 days.

At weeks 7, 17, and 27 the subject will receive Ara-C as a continuous infusion for 72 hours (higher dose) or injected under the skin (lower dose). VM-26 will be given as a 45-minute IV infusion before the start of Ara-C and on day 2 with standard dose Ara-C. If the subject receives intensified Ara-C, the subject will also receive the drugs PEG and G-CSF. PEG is a drug that may lessen the toxic effects of Ara-C, and G-CSF is used to increase the blood count to decrease the risk of infection.

At weeks 12, 22, and 32, Ara-C will be infused over 72 hours as described above. Daunomycin (DNR) will be given as a 30-minute infusion before the start and at the end of the Ara-C. In addition to DNR/Ara-C, vincristine is given IV on days 1 and 8, prednisone by mouth on days 1 and 7, and PEG-L-asparaginase IM on day 1.

During the period known as continuation, weeks 35-130, standard dose 6-MP will be given orally each day, and methotrexate injected into a muscle (IM) once a week. The total time of planned therapy is 130 weeks (2 1/2 years).

The subject will be taken off study in case of relapse in the bone marrow, or any other site, or if the subject fails to achieve a complete remission during the induction phase of the study. Radiation therapy will be suggested if the subject has CNS leukemia at diagnosis.

At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may be used for research studies.

Progress: No patients were enrolled in FY 97. One patient was enrolled in this study in FY 96, however due to an adverse event during induction he was taken off study; however, is still receiving therapy. Another patient accepted in transfer from SUNY relapsed while on therapy. Both continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/072		<b>Status:</b> Completed	
<b>Title:</b> POG 9411: SIMAL 9: Treatment of Relapsed Non-T, Non-B Acute Lymphoblastic Leukemia with Intensive Chemotherapy					
<b>Start Date:</b> 02/16/96			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:leukemia, pediatric, chemotherapy					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/21/97	

**Study Objective:** 1) To determine the feasibility and toxicity of delivering an intensive reinduction and consolidation chemotherapy regimen for children with acute lymphoblastic leukemia (ALL) following first bone marrow relapse; 2) to compare the induction response rates for patients randomized to weekly PEG versus 3 times a week E. coli asparaginase; 3) to study the induction of blast cell p53, p21 and GADD45 genes in relapsed ALL and correlate with the results of *in vitro* and *in vivo* responses to cytotoxic therapy; 4) to study somatic cell mutations in children with relapsed ALL undergoing intensive chemotherapy; and 5) to compare remission rate, toxicity, and Asparaginase levels in children treated with Peg L-Asparaginase compared to E. Coli Asparaginase during induction and continuation therapy for relapsed ALL.

**Technical Approach:** Patients will be randomized at registration to PEG-L-Asparaginase (Treatment 01) or E. Coli Asparaginase (Treatment 02) or non-randomly to PEG-L-asparaginase (Treatment 01) if there was prior hypersensitivity to E. Coli Asparaginase. Reinduction therapy will consist of a four drug regimen of doxorubicin, prednisone, vincristine and PEG-L or E. Coli Asparaginase. Intrathecal prophylaxis will be given to patients with or without CNS involvement. Consolidation will consist of non-cross-resistant drug combinations to include Ifosfamide/VP-16/MESNA and Ara-C/Idarubicin. Continuation therapy will include 5 cycles each consisting of four courses of different drug combinations using VP-16/Ifos/MESNA; 6-thioguanine/methotrexate; idarubicin/Ara-C and dexamethasone/vincristine/PEG-L-asparaginase.

**Progress :** One patient was enrolled in this study at MAMC in FY 97; however, he died of the disease. Study was closed to patient accrual 15 April 97.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/089		<b>Status:</b> On-going	
<b>Title:</b> POG 9421: Phase III Evaluation of Standard vs. High Dose ARA-C Induction Followed by the Randomized Use of Cyclosporine A As An MDR Reversal Agent, Compared to Allogeneic BMT, in Childhood AML					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Jan 01		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:AML, ARA-C, Cyclosporine, multidrug resistance					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/21/97

Study Objective: 1) To determine the effect of high dose vs. standard dose Ara-C induction on CR (clinical remission) and EFS (event free survival) in Childhood AML. 2) To compare EFS in Childhood AML after 3 cycles of consolidation with or without the MDR (multidrug resistance) modulator CSA (cyclosporine A). 3) To compare the EFS between patients genetically randomized between allogeneic BMT and chemotherapy. 4) To evaluate the impact of EFS of various clinical and laboratory factors such as cytogenetics and MDR expression. 5) To confirm the superior response of Down syndrome patients utilizing standard induction and non-CSA containing consolidation, and identify specific biologic and pharmacokinetic characteristics in these patients.

Technical Approach: Phase III evaluation of standard vs. high dose Ara-C induction followed by the randomized use of Cyclosporine A as an MDR (multidrug resistant) reversal agent, compared to allogeneic BMT, in childhood AML. Patients will be randomized (assigned by chance, such as flipping a coin) at the time of diagnosis to receive either standard doses or high doses of ARA-C during the initial course of therapy. The chances of receiving any of the therapies is approximately equal. Later in the course of therapy, patients (according to how they were previously randomized) will or will NOT receive the drug Cyclosporine A in combination with the chemotherapy agents, Mitoxantrone and Etoposide. Patients with Down syndrome will not be randomized, but will receive the standard therapy. Earlier studies have shown the three year event-free survival rate for Down syndrome children significantly superior to children without Down syndrome using standard therapy. Also, for this reason Down syndrome patients will not receive Cyclosporine A. If a sibling who is matched for bone marrow transplantation, will receive bone marrow transplantation, which has been shown to be a more effective treatment in controlling AML compared to chemotherapy, providing that consent from the sibling donor can be obtained. If not a sibling donor, studies have shown chemotherapy is superior to matched unrelated donor BMT. However, should the patient choose to pursue an unrelated matched BMT instead of continuing with consolidation chemotherapy, the subject may discontinue the study. At the time of bone marrow aspiration, blood sampling, or spinal tap, cells obtained may also be used for research studies.

Progress : No patients were enrolled in FY 97. One patient accepted in transfer from WRAMC is off protocol therapy and continues to be followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/071		<b>Status:</b> On-going	
<b>Title:</b> POG 9425: Advanced Stage Hodgkin's Disease, A Pog Phase III Study					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Jul 03		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:Hodgkin' disease, doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide, dexrazoxane					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) To test the efficacy of DBVE-PC, an intensive treatment regimen for advanced stage Hodgkins disease that administers doxorubicin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide with G-CSF at 3 week intervals in a dose intensive manner (using cumulative drug doses that may minimize long term toxicity), followed by consolidative radiotherapy; 2) To tailor therapy based on rapidity of response in order to minimize cumulative drug dosages. Those in CR after 3 cycles of DBVE-PC will receive only low dose RT. Those who are not in CR will receive 2 additional cycles of DBVE-PC (+ low dose RT); 3) To determine, in a randomized trial, whether the addition of Dexrazoxane reduces pulmonary and cardiac toxicity of DBVE-based therapy without compromising response.

**Technical Approach:** This randomization will include all patients with Hodgkins's disease on POG 9425 (advanced stage) and 9426 (early stage) or not to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 3 cycles of the drug combination etoposide, vincristine, bleomycin, doxorubicin cyclophosphamide, prednisone combination with G-CSF in 3 week intervals. Patients will be restaged after receiving these three chemotherapy courses. Those showing large tumor response will go on to radiation therapy, while those showing partial response will receive 2 additional cycles of chemotherapy and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis after completion of therapy.

**Progress :** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/054		<b>Status:</b> On-going	
<b>Title:</b> POG 9426: Response Dependent Treatment of Stages IA, IIA, and IIIA(1-micro) Hodgkin's Disease with DBVE and Low Dose Involved Field Irradiation with or without Zinecard					
<b>Start Date:</b> 02/21/97			<b>Est. Completion Date:</b> Jul 03		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:Hodgkin's, Zinecard, Irradiation					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	/ /		

**Study Objective:** 1. To tailor chemotherapy courses based on the patients' initial response to therapy; 2) To examine the activity of variable courses of doxorubicin, bleomycin, vincristine, and etoposide (DBVE) and low-dose involved field irradiation; 3) To monitor safety and feasibility of the response-dependent approach, and morbidity, immediate and long term toxicities of the above regimen; 4) To evaluate if limited therapy is adequate for patients with early response; 5) To examine if addition of Zinecard can reduce pulmonary toxicity while not significantly reducing response rate or event-free survival; 6) To determine if the frequency and magnitude of myocardial injury during therapy, as measured by an elevation of cardiac Troponin-T in the serum, is reduced by the addition of Zinecard.

**Technical Approach:** Registered study patients will be randomized to receive the investigational drug Zinecard just prior to the administration of the chemotherapy drugs bleomycin and doxorubicin. Following disease staging with radiologic imaging and laboratory evaluations, patients will receive 2 courses of the four drug combination etoposide, vincristine, bleomycin and doxorubicin at 28 day intervals. Patients will be restaged after receiving these two chemotherapy courses. Those showing remission will go on to radiation therapy, while those showing residual disease will receive 2 more courses of the four drug combination and then go on to radiation therapy. Follow-up will continue for a minimum of 10 years at least on a yearly basis.

**Progress :** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/097		<b>Status:</b> On-going	
<b>Title:</b> POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> Jul 02		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>   LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:Wilms, chemotherapy, radiation therapy, biology study					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		04/18/97	

**Study Objective:** 1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood; 2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor; 3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor; 4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis; 5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor; 6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide; 7) to improve survival of patients with malignant rhabdoid tumor of the kidney; 8) to study biology and pathology of patients who present with bilateral Wilms tumor; 9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines; and 10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine.

**Technical Approach:** Wilms tumor is the most frequent malignant renal tumor in children. This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages 1-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.

**Progress:** One patient was enrolled in this study at MAMC in FY 96 and was transferred to Portsmouth Naval Hospital. No new patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/186		<b>Status:</b> Completed	
<b>Title:</b> POG 9450: Etoposide/Ifosfamide + G-CSF in the Treatment of Newly Diagnosed Metastatic Osteosarcoma or Unresectable Osteosarcoma					
<b>Start Date:</b> 09/15/95			<b>Est. Completion Date:</b> Jan 99		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>					
LTC Luke M. Stapleton, MC			LTC Shirley E. Reddoch, MC		
LTC Robert B. Ellis, MC			LTC Kenneth A. Bertram, MC		
LTC Robert D. Vallion, MC			MAJ James S. D. Hu, MC		
MAJ John R. Caton, MC			MAJ Richard F. Williams, MC		
			LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:osteosarcoma, etoposide, ifosfamide, G-CSF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>//</b>

**Study Objective:** 1) To estimate the response rate to etoposide (VP-16), ifosfamide (IFOS) and G-CSF in patients presenting with newly-diagnosed metastatic or unresectable osteosarcoma prior to treatment with other chemotherapeutic agents. 2) To evaluate the toxicity of VP-16/IFOS in newly diagnosed patients. 3) To estimate the duration of survival for patients presenting with newly-diagnosed metastatic osteosarcoma or unresectable osteosarcoma who are treated with a multi-agent chemotherapy regimen preceded by induction therapy with VP-IFOS and G-CSF. 4) To determine the ability of pathologic primary tumor response from 2 courses of pre-surgical chemotherapy to predict outcome as measured by time to disease progression, disease free survival and survival.

**Technical Approach:** This study involves treatment with the combination of drugs etoposide (VP-16) and ifosfamide (IFOS) at high doses. Granulocytic Colony Stimulating Factor (G-CSF) will be used to help the patient's bone marrow white cells recover faster after each of the first 2 courses of high dose VP-16 and IFOS, and thereafter as necessary. This study will determine the response rate of high dose VP-16/IFOS in the treatment of osteosarcoma and will try to determine whether this high dose combination will improve the overall outcome of this group of high risk patients. Patients will also receive these drugs in standard dosing during continuation therapy in combination with other chemotherapy drugs which are used to treat osteosarcoma. VP-16 will be given intravenously over 60 minutes, followed by intravenous ifosfamiti over 4 hours every day for 5 days. Another drug, MESNA will also be given at specified intervals with and after ifosfamide. The purpose of MESNA is to help prevent bleeding from the bladder which can occur with ifosfamide. G-CSF will be given subcutaneously (injected under the skin) once a day, starting on the day the chemotherapy finishes and continuing until blood counts return to normal. This course will be repeated one more time (approximately 3 weeks later). After 6 weeks, patient will be re-evaluated (x-ray, MRI, CT) to determine the response to this drug combination. If possible, all sites of remaining tumor will then be removed surgically. After surgery, chemotherapy will resume with a combination of drugs (methotrexate. ifosfamide. VP-16 adriamycin and cisplatin) which have been proven to be effective against osteosarcoma. The vitamin Calcium Leucovorin will be given along with the methotrexate. Treatment will then continue for approximately one year.

**Progress:** Closed to patient accrual 15 Sept 97. No patients were enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/039	<b>Status:</b> On-going
<b>Title:</b> POG 9457: Intensive Therapy with Growth Factor Support for Patients with Ewing's Tumor Metastatic at Diagnosis		
<b>Start Date:</b> 12/15/95	<b>Est. Completion Date:</b> Sep 99	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	LTC Shirley E. Reddoch, MC	
LTC Robert B. Ellis, MC	LTC Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	MAJ James S. D. Hu, MC	
MAJ John R. Caton, MC	MAJ Richard F. Williams, MC	
	LTC Kelly J. Faucette, MC	
<b>Key Words:</b> Cancer:Pediatric Ewing's, Topotecan, ifosfamide, etoposide, vincristine, adriamycin, cyclophosphamide, G-CSF, interleukin-6		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/21/97

**Study Objectives:** (1) To evaluate the response rate, and duration of response in patients with Ewing's tumor, metastatic at diagnosis, treated with maximally intensified therapy. (2) To evaluate the response to new agents utilized in an upfront window. Initially, topotecan will be used as a single agent. When the maximally tolerated dosages of the combination of topotecan and cyclophosphamide are available, the combination will be employed. (3) To assess the role of surgical treatments with regard to local control of primary and metastatic sites and disease course. (4) To determine whether individual variability in ifosfamide and cyclophosphamide metabolism correlated with toxicity and/or response. (5) To evaluate the rise in the absolute neutrophil count following one dose of G-CSF just prior to a chemotherapy cycle as a measure of bone marrow reserve and subsequent myelosuppression.

**Technical Approach:** In the absence of effective new agents in Ewing's Tumor, attempts to increase the rate of cure have recently centered around increasing dose intensity. Ifosfamide will be used at a dosage level 25% higher than that currently being used, for the first 3 cycles. The dosage will be reduced for the 2 continuation cycles. Cyclophosphamide will also be used in increased dosage with vincristine and adriamycin. This study will encourage the use of surgery for local control, with irradiation of the primary tumor bed, unresectable primary tumors and selected metastatic sites. Topotecan is a camptothecin, a topoisomerase I inhibitor. Initially, this study will use 2 cycles of single agent topotecan 3 weeks apart. At least 14 patients will be registered. When the maximum tolerated dosages of the combination of topotecan and cyclophosphamide are available, subsequent patients will be treated with the combination.

**Progress:** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/143		<b>Status:</b> On-going	
<b>Title:</b> POG 9485: Intergroup Protocol, Assessmentof the Role of Minimal Access Surgery in the Treatment of Childhood Cancer: Intergroup Laparoscopy Protocol					
<b>Start Date:</b> 07/19/96			<b>Est. Completion Date:</b> Jul 98		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> MAJ Randall M. Holland, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Cancer:solid tumor, pediatric, laparoscopy, QOL					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>	\$0.00	07/18/97

**Study Objective:** 1) To investigate the role of minimal access abdominal surgery (MAS) in terms of the perioperative complication rate and the mortality rate; 2) to compare the impact of MAS and open laparotomy on quality of life (QOL). Several domains of QOL will be examined including surgery-related pain, physical, social and emotional functioning, and global ratings of health and overall QOL; 3) to compare the impact of MAS and open laparotomy on economic costs; 4) to compare the complete tumor resection rate for MAS with open surgery within specific diagnostic groups; 5) to assess the impact of minimal access surgery on compliance with specimen eligibility requirements for therapeutic protocols.

**Technical Approach:** Pediatric patients less than or equal to 21 years old who require surgery to obtain biopsy material, lymph node sampling for staging, liver biopsies, tumor excisions, organ excision, second-look procedures, etc., will be considered for entry and will be randomized to either open or a minimal access procedure. Protocol eligibility is linked with the requirement to obtain adequate surgical specimens. MAS offers the potential to minimize a potential barrier to enrollment onto protocol therapy. Biologic specimens will be assessed for their adequacy in terms of both the specimen quantity and quality. Demographic data, procedural and overall economic costs, operative time, anesthesia and post-operative analgesia, length of post-operative stay, interval between procedure and subsequent actions, and perioperative morbidity will all be evaluated. Methods of evaluations will include Quality-of-Life assessment, Pain Ratings, Play-Performance/Karnofski assessment, operative and overall mortality, surgery characteristics, radiology review and imaging guidelines.

**Progress:** No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/035		<b>Status:</b> On-going	
<b>Title:</b> POG 9490: Topotecan Followed by Multimodal, Multiagent Therapy for Children and Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study					
<b>Start Date:</b> 11/17/95			<b>Est. Completion Date:</b> Jun 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:pediatric rhabdomyosarcoma, Topotecan					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/15/96

**Study Objectives:** (1) To evaluate the toxicity of the topoisomerase I inhibitor, topotecan, when given alone at a maximum tolerated dose by bolus injection daily X 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease. (2) To estimate the response rate (complete or partial) of such patients to topotecan. (3) To evaluate the toxicity of a new chemotherapy combination comprising topotecan, cyclophosphamide, and vincristine (VTC) given in alternating cycles with vincristine, actinomycin D, and cyclophosphamide (VAC) to patients who have achieved an objective response partial response (PR) or complete response (CR) to topotecan.

**Technical Approach:** Patients with rhabdomyosarcoma, clinical stage IV disease will receive Topotecan upfront at 2.0 mg/M<sup>2</sup>/day X 5 IV. Following evaluation, patients with partial response or complete response will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 in conjunction with vincristine and cyclophosphamide. Continuation therapy begin following evaluation at week 25 with VAC/VTC for patients showing PR and CR.

**Progress:** Closed to patient accrual 1 Nov 96. One patient was enrolled in this study at MAMC in FY 96 and continues to be followed. No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/015		<b>Status:</b> On-going	
<b>Title:</b> POG 9150/CCSG 6901 - Intergroup Rhabdomyosarcoma Study-IV for Stage I Disease.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Rhabdomyosarcoma					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/15/96

**Study Objectives:** To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytosine (VAC) vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to: a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

**Technical Approach:** This is a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen for Stage 1 disease, excluding Clinical Group I paratesticular and Groups I and II orbit/eyelid patients, in IRS-IV. The modifications of VAC involve maximizing its intensity: cytosine is delivered in a single high dose rather than at a lower dose daily x 3, actinomycin-D is delivered more frequently in induction, and VCR more frequently during continuation. The two experimental arms differ from the control in that ifosfamide is substituted for cytosine in one (VAI) and ifosfamide + VP-16 are substituted for actinomycin-D + cytosine in the other (VIE). The comparison then, is VAC vs VAI vs VIE. Clinical Group I paratesticular and orbit/eyelid patients will be treated separately with VA alone. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2, and 3 patients with gross residual disease after surgery (clinical group III). Within each stage, except for stage 4 radiotherapy will be randomized or assigned by Clinical Group. Participation in the corresponding tumor study (PO #9153) is required.

**Progress:** No patients were enrolled in FY 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/016		<b>Status:</b> On-going	
<b>Title:</b> POG 9151/CCSG 6902 - Intergroup Rhabdomyosarcoma Study-IV for Stage II and Stage III Diseases.					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> JUN 97		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> COL Bruce A. Cook, MC			LTC Shirley E. Reddoch, MC LTC Kelly J. Faucette, MC		
<b>Key Words:</b> Rhabdomyosarcoma					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					11/21/97

**Study Objectives:** To compare the progression-free survival rates of patients receiving vincristine-actinomycin-D-cytosin (VAC) vs patients receiving vincristine-actinomycin-D-ifosfamide (VAI) vs those receiving vincristine-ifosfamide-etoposide (VIE) for treatment of rhabdomyosarcoma and undifferentiated sarcoma. To compare hyperfractionated radiation therapy (RT) to conventional RT in regard to a) local relapse rates, and b) early/acute toxicity and late effects. To investigate the relationship between immunohistochemical pattern of tumor and prognosis, and to evaluate newly identified immunohistochemical markers in diagnosis. To correlate clinical features of disease and prognosis with tumor cytogenetics, DNA index and amplification or rearrangement of specific cellular proto-oncogenes. To provide a bank of frozen tumor tissue for use in tumor biology studies. To evaluate the use of recombinant G-CSF as a supportive measure for ameliorating hematopoietic toxicity.

**Technical Approach:** This study is designed to determine whether an ifosfamide-based combination (VAI) is superior to a cyclophosphamide-based combination (VAC) in previously untreated patients. Therefore, a randomized 3-arm study with an internal control consisting of a modified repetitive pulse VAC regimen is the study to be undertaken for stages 2 and 3 disease in IRS-IV. The two experimental arms (VAI and VIE) differ from the control arm as follows: ifosfamide is substituted for cyclophosphamide in one cyclophosphamide in the other (VIE). The comparison then, is VAC vs VAI vs VIE in IRS-IV. The second major comparison and randomization in IRS-IV will be between conventional RT and hyperfractionated RT (Hyperfx-RT) in stages 1, 2 and 3 patients with gross residual disease after surgery (clinical group III). The goal is to try to improve the local control rate in these Group III patients with Hyperfx-RT, whereas Group II patients in these stages have an acceptable local control rate of 90% with conventional RT and will continue to receive conventional RT in IRS-IV.

**Progress:** No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/089	<b>Status:</b> On-going
<b>Title:</b> POG 9553: A Phase II of Neoadjuvant Vincristine, Ifosfamide, Doxorubicin, and G-CSF in Children with Advanced Stage Non-rhabdomyosarcoma Soft Tissue Sarcomas		
<b>Start Date:</b> 04/18/97	<b>Est. Completion Date:</b> Jul 03	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC		
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC		LTC Shirley E. Reddoch, MC
<b>Key Words:</b> Cancer:soft tissue sarcoma, vincristine, ifosfamide, doxorubicin, cyclophosphamide		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

Study Objective: 1) To estimate the response rate to the combination of vincristine, ifosfamide, and doxorubicin (VID), with G-CSF support, in children with newly diagnosed inoperable or metastatic nonrhabdomyosarcoma soft tissue sarcomas; 2) To estimate the 2-year survival and event-free survival of children treated with VID in combination with radiotherapy and/or surgery; 3) To establish a bank of frozen tissue (tumor and peripheral blood) for use in further molecular studies .

Technical Approach: Registered study patients will receive the three drug combination Vincristine, Ifosfamide, and Doxorubicin; two courses within a 6 week period. Cyclophosphamide will be substituted for those patients who cannot tolerate Ifosfamide. Patients will then be evaluated for response. If the tumor shrinks, patients will go on to XRT/chemotherapy, with or without prior surgical resection at this time. If the tumor has grown or stayed the same, patients will be taken off study treatment and offered other therapy. After XRT and chemotherapy, patients will be reimaged and another six weeks of chemotherapy will be given at this time unless the tumor has grown or come back.

Progress : No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/120		<b>Status:</b> On-going	
<b>Title:</b> POG 9605: ALinC 16: Protocol for Patients With Newly Diagnosed Standard Risk Acute Lymphoblastic Leukemia (ALL)					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Jul 03		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:leukemia, lymphoblastic, methotrexate, 6-mercaptopurine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	05/16/97		

**Study Objective:** 1) To determine in a randomized trial whether the addition of 6 months of delayed intensification with divided dose oral methotrexate (ddMTX) improves event-free survival (EFS) of children with standard risk acute lymphoblastic leukemia; 2) to determine in a randomized trial the effect on EFS of delivering oral 6-mercaptopurine (6-MP) on a divided (twice daily) vs once a day schedule, during delayed intensification and continuation; 3) to study how laboratory data from POG 9400 correlates with outcome by pooling studies 9201, 9405, 9605, and 9406; 4) to assess the prognostic significance of the percent of marrow blasts after two weeks of induction therapy; 5) to describe the occurrence of elevated transaminases and correlation of these with outcome.

**Technical Approach:** This treatment protocol involves 130 weeks of chemotherapy beginning with standard induction therapy of generally 4 (but up to 6) weeks of chemotherapy consisting of vincristine, prednisone, and L-asparaginase plus triple intrathecal therapy of combined methotrexate, hydrocortisone and Ara-C. Post induction, the treatment is divided into consolidation, intensification, and maintenance phases of therapy. Registration on study occurs post induction therapy at which time patients are randomized to receive 1 of 4 regimens which vary beginning in the intensification phase of therapy.

**Progress:** No patients were enrolled in FY 97. One patient was enrolled in this study at MAMC in FY 96 transferred to WRAMC. One patient accepted in transfer from SUNY continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/088	<b>Status:</b> On-going
<b>Title:</b> POG A9961: A Phase III Prospective Randomized Study of Craniospinal Radiotherapy Followed by one of Two Adjuvant Chemotherapy Regimens (CCNU, CDDP, VCR, or CPM, CDDP, VCR) in Children with Newly-....		
<b>Start Date:</b> 04/18/97	<b>Est. Completion Date:</b> Apr 03	
<b>Department:</b> POG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC		
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC		LTC Shirley E. Reddoch, MC
<b>Key Words:</b> Cancer:Medulloblastoma, cyclophosphamide, CCNU, vincristine, cisplatin, radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

**Study Objective:** 1) To determine if a cyclophosphamide arm will increase the rate of progression-free survival compared to a CCNU containing arm for children with average-risk medulloblastoma; 2) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of 5580 cGy, and adjuvant vincristine, CCNU and cisplatin chemotherapy; 3) To determine the progression-free survival and overall survival of children treated with craniospinal (2340 cGy) and local boost radiotherapy (3240 cGy) for a total dose of 5580 cGy, and adjuvant vincristine, cyclophosphamide and cisplatin chemotherapy; 4) To determine the long-term neurocognitive, endocrinologic and cardiopulmonary sequelae of radiotherapy plus adjuvant chemotherapy in children with average-risk medulloblastoma treated with 2340 cGy of craniospinal radiation therapy, local boost radiotherapy, and either one of two drug regimens and to determine if the replacement of CCNU with cyclophosphamide will alter the incidence and degree of sequelae experienced; 5) To determine if cellular/biologic parameters, including tumor molecular genetic analysis, DNA ploidy, mitotic activity markers and immunohistochemical analysis are correlated with progression-free survival, survival and the pattern of disease relapse in children with average-risk medulloblastoma; 6) To determine the utility of routine MR surveillance studies of the head and spine to detect subclinical recurrent disease

**Technical Approach:** Following surgery, patients will be randomized to receive Regimen A or B of treatment. Both regimens will include 2340 cGy of craniospinal radiation and 3240 cGy of boost radiation directly to the primary tumor with weekly vincristine doses. Six weeks following the completion of radiotherapy, patients will begin 8 cycles of maintenance chemotherapy for Regimen A (CCNU, cisplatin and vincristine) or Regimen B (cyclophosphamide, cisplatin and vincristine). The study is expected to accrue between 240 and 300 patients over a minimum of 4 year accrual period.

**Progress :** No patients were enrolled in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/090		<b>Status:</b> On-going	
<b>Title:</b> POG D9501: Topotecan and Cyclophosphamide, Followed by Multimodel, Multiagent Therapy for Children & Adolescents with Newly Diagnosed Stage IV/Clinical Group IV Rhabdomyosarcoma, an IRS-V Pilot Study					
<b>Start Date:</b> 04/18/97			<b>Est. Completion Date:</b> Jul 03		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b> LTC Kelly J. Faucette, MC			LTC Shirley E. Reddoch, MC		
<b>Key Words:</b> Cancer:rhabdomyosarcoma, actinomycin D, cyclophosphamide, topotecan, vincrsitine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		/ /	

**Study Objective:** 1) To evaluate the toxicity of cyclophosphamide and the topoisomerase I inhibitor, topotecan, when given together by 30 minute infusion daily x 5 days/course for 2 courses to untreated children and adolescents with Stage IV and/or Clinical Group IV rhabdomyosarcoma, all patients with metastatic disease; 2) To estimate the response rate (complete or partial) of such patients to cyclophosphamide and topotecan; 3) To evaluate the toxicity of a new chemotherapy combination comprising vincristine (VCR), cyclophosphamide, and topotecan given in alternating cycles with vincristine, dactinomycin, and cyclophosphamide (VAC) to patients who have achieved an objective response, partial response (PR) or complete response (CR) to topotecan.

**Technical Approach:** Patients with advanced stage rhabdomyosarcoma will receive two courses of Topotecan & Cyclophosphamide upfront. Following evaluation patients with partial response (PR) or complete response (CR) will go on to VAC treatment, alternating with VTC treatment. Those with stable or progressive disease will proceed to VAC alone. Radiation therapy will begin following evaluation at week 15 and in conjunction with vincristine and cyclophosphamide. Continuation therapy begins following evaluation at week 25 with VAC/VTC for patients showing PR and CR; and VAC alone for patients with stable or progressive disease. Patients will be evaluated again at week 44.

**Progress :** No patients were enrolled in FY 97.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/145		<b>Status:</b> On-going	
<b>Title:</b> POG D9602: Actinomycin D and Vincristine with or without Radiation Therapy for Newly Diagnosed Patients with Low-Risk Rhabdomyosarcoma or Undifferentiated Sarcoma: An IRS-V Protocol					
<b>Start Date:</b> 09/19/97			<b>Est. Completion Date:</b> Jul 03		
<b>Department:</b> POG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Stephen R. Palmer, MC					
<b>Associate Investigators:</b>			LTC Kelly J. Faucette, MC		
<b>Key Words:</b> cancer:rhabdomyosarcoma, cancer:undifferentiated sarcoma, pediatric, actinomycin D, vincristine, radiation therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> / /

**Study Objective:** 1) Treatment of IRS-V low-risk patients with actinomycin D (AMD) and vincristine (VCR), plus local radiotherapy (XRT) for microscopic or gross residual tumor, will result in a failure-free survival rate of 88% at 2 years and an overall survival rate of about 95% at 5 years from initial diagnosis; 2) Treatment of IR8-V low-risk patients with alveolar rhabdomyosarcoma or undifferentiated sarcoma with vincristine and actinomycin D plus cyclophosphamide (collectively called VAC) will result in a failure-free survival rate of greater than or equal to 70% at two years and an overall survival rate of about 80-90% at 5 years; 3) Reduction in radiation therapy dose for patients with Clinical Group II disease to 36 Gy (from 41.3 Gy) and for Group III patients with orbital disease to 45 Gy (from 50-Gy) will result in local control rates of about 90%.

**Technical Approach:** Patients in Group I have no residual tumor following surgery and will receive no radiation therapy. Patients in Group II have microscopic residual tumor and will receive radiation therapy at a dose lower than the current standard. Patients in Group III, orbit tumor only, have visible residual tumor after biopsy and will receive radiation therapy. The results will be compared to current intergroup rhabdomyosarcoma study results.

All patients will begin chemotherapy with the two-drug combination of vincristine and actinomycin D, given over a 3-week period while their tumor specimen is being classified at the IRS Group Pathology Center in Columbus, Ohio.

Patients whose tumor is classified as embryonal or botryoid rhabdomyosarcoma will continue to receive vincristine and actinomycin D, given at weeks 12 through 21, 24 through 33, and 36 through 45.

Patients whose tumor is classified as alveolar rhabdomyosarcoma or undifferentiated sarcoma will have the chemotherapy drug cyclophosphamide added to the combination of vincristine and actinomycin D, given at weeks 3, 6, 9, 12, 15, 18, 24, 27, 30, 36, and 42. Cyclophosphamide will be added on Week 0 for these patients who show molecular genetic or cytogenetic evidence of the t(2;13) or t(1;13) translocation, or the PAX 3-FRHR or PAX 7-FRER gene fusion product.

**Progress :** No patients were enrolled in FY 97.

**DETAIL SHEETS FOR PROTOCOLS**

**RADIOLOGICAL DIAGNOSTIC ONCOLOGY  
GROUP**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/136		<b>Status:</b> On-going	
<b>Title:</b> RDOG(5) 6881: Stereotactic Fine Needle Aspiration Biopsy and Core Needle Biopsy in the Work-up of Lesions Detected by Mammography					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> RDOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Donald V. Smith, MC					
<b>Associate Investigators:</b> MAJ Vincent B. Ho, MC Preston L. Carter, M.D. CPT Janice C. Stracener, MC			Charlene P. Holt, M.D. LTC William C. Williard, III, MC MAJ Barbara A. Crothers, MC COL Sankaran S. Babu, MC		
<b>Key Words:</b> Cancer:breast, FNA, Core biopsy, mammography					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
<b>Periodic Review:</b>					06/21/96

**Study Objectives:** The overall objective of this research protocol is to conduct a randomized clinical trial to study whether stereotactically-guided and/or ultrasound-guided fine needle aspiration (FNA) and/or core needle biopsy (CNB) can replace open surgical biopsy in the diagnostic evaluation of nonpalpable mammographically-detected breast lesions.

**Technical Approach:** This is a randomized clinical trial to be carried out in mammographic centers nationwide within two consortia. This offers the opportunity to cover the spectrum of experience, equipment and patient populations, all using an agreed protocol to evaluate the use of fine needle and core biopsy used in the work-up of non-palpable breast lesions. The two consortia will enroll a total of 3,600 patients with an expected average MAMC enrollment of two subjects per day for the length of the study. Women having had the appropriate mammographic evaluation and meeting the inclusion criteria will be entered either to stereotactic or ultrasound arms of the study. Those in the stereotactic arm will be randomized to FNA followed by CNB, or CNB alone, both followed by open surgical biopsy or when indicated, 6, 12, and 24 month follow-ups. Those in the ultrasound arm will be randomized to FNA/CNB or CNB. All mammograms will have second readings by experts, and all pathology and cytology will have second readings by reference experts. Data analysis will consist of accuracy determination, agreement analysis, and logistic regression modeling for evaluation of important co-variants on the estimates. In addition, analysis of observer variability, insufficient sample rates, and predictive ability of specific mammographic characteristics will be conducted.

**Progress:** Study is closed to patient entry. 38 subjects entered at MAMC, following subjects with the last patient finishing in October 1998.



**DETAIL SHEETS FOR PROTOCOLS**

**SOUTHWEST ONCOLOGY GROUP**

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 77/054		<b>Status:</b> On-going
<b>Title:</b> SWOG 7406: Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III				
<b>Start Date:</b> 02/18/77		<b>Est. Completion Date:</b> Feb 82		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC		LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:Hodgkin's, MOPP				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	02/21/97	

**Study Objective:** (1) To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy; (2) To evaluate systematic restaging of patients in apparent complete remission; (3) To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging; (4) To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

**Technical Approach:** All previously untreated patients with Ann Arbor Stages IIIB or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission (PR) is indicated another 4 courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

**Progress:** Closed to patient entry 31 Aug 78. Two patients where entered in previous years, one patient is still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 77/053		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7433: Non-Hodgkin's Lymphomas (Stages I, IE, II, and IIE). A Phase III Study.					
<b>Start Date:</b> 02/18/77			<b>Est. Completion Date:</b> Feb 82		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC			LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, radiotherapy, CHOP					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 02/21/97

**Study Objective:** To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, IE, II and IIE treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone or with extended Hydroxyl-daunorubicin (adriamycin), Oncovin (vincristine), and Prednisone.

**Technical Approach:** Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

**Progress:** This protocol was closed to patient entry 1 Oct82 and was previously reported as closed. In fact, 2 patients were entered at MAMC, 1 has died and the other is still being followed. The protocol was reactivated in December 1993 in order to allow SWOG to continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 77/024		<b>Status:</b> On-going
<b>Title:</b> SWOG 7436: Combined Modality Therapy of Breast Cancer				
<b>Start Date:</b> 01/21/77		<b>Est. Completion Date:</b> Jan 82		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> LTC H. Irving Pierce, MC		COL Friedrich H. Stutz, MC		
<b>Key Words:</b> Cancer:breast, 5-FU, vincristine, methotrexate, cyclophosphamide, prednisone				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		02/21/97

**Study Objective:** To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

**Technical Approach:** Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater than six weeks for entry into the study. All therapy will be discontinued after one year.

**Progress:** This protocol was closed to patient entry in 1 Nov 1979 and was previously reported as closed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on 10 patients that had been entered. One patient expired in FY 97. 18 years after treatment. Five other patients expired previously and four patients are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 77/018		<b>Status:</b> On-going
<b>Title:</b> SWOG 7510: Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel				
<b>Start Date:</b> 10/15/76		<b>Est. Completion Date:</b> Oct 81		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC		LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:bowel, chemotherapy, BCG immunotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		11/17/95

Study Objective: To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Suerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

Technical Approach: Patients will be randomly assigned to either of the two following regimens; (1) chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would be every eight weeks; (2) chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

Progress: This protocol was closed to patient entry 20 Aug 1980 and was previously reported as closed. 11 patients were entered at MAMC, 8 have died, 3 are still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 78/002		<b>Status:</b> On-going
<b>Title:</b> SWOG 7713/14: Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance After Remission Induction				
<b>Start Date:</b> 10/21/77		<b>Est. Completion Date:</b> Jun 79		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC		LTC H. Irving Pierce, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, CHOP, Levamisole, BCG				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		11/17/95

**Study Objective:** (1) To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma; (2) For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy; (3) For patients with impaired cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole; (4) To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used; (5) To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases; (6) To establish baseline and serial data on immunologic status in bother chemoimmunotherapy groups.

**Technical Approach:** Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac disease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or impaired bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

**Progress:** This protocol was closed to patient entry 1 Oct 1982 and was previously reported as completed. 4 patients were entered at MAMC, 3 have died, one patient is still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 78/047		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7808: Combination Modality Treatment for Stage III and Stage IV Hodgkin's Disease, MOPP #6					
<b>Start Date:</b> 07/31/78			<b>Est. Completion Date:</b> Jan 88		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> LTC H. Irving Pierce, MC			COL Friedrich H. Stutz, MC Suresh B. Katakhar, M.D., DAC		
<b>Key Words:</b> Hodgkin's disease:Stages III & IV,chemotherapy,modality RX					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		11/17/95

**Study Objective:** To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

**Technical Approach:** Patients (>15 yrs) must have histologic diagnosis of Hodgkin's disease; no prior chemotherapy. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease will be excluded. Normal marrow patients will receive six cycles of MOP-BAP. Impaired bone marrow patients will receive six cycles of MOP-BAP with dose modifications. Complete Remission (CR) patients with prior radiotherapy will be randomized to Treatment 3 (no treatment) or Treatment 4 (levamisole). CR patients without prior radiotherapy will receive Treatment 5 (radiotherapy). Partial remission (PR) patients without prior radiotherapy or residual bone marrow involvement will receive Treatment 6 (radiotherapy). PR patients with prior radiotherapy or those with residual bone marrow involvement will receive Treatment 7 (4 additional cycles of MOP-BAP); after 10 total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator.

**Progress:** This study was closed to patient entry 1 Dec 87. Thirteen patients were enrolled in previous years and 5 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 79/096		<b>Status:</b> On-going	
<b>Title:</b> SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III					
<b>Start Date:</b> 09/21/79			<b>Est. Completion Date:</b> Sep 81		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> Suresh B. Katakhar, M.D., DAC			COL Friedrich H. Stutz, MC COL Irwin B. Dabe, MC		
<b>Key Words:</b> cancer:breast,chemotherapy,modality therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/17/95

**Study Objective:** To compare the disease-free interval and recurrence rates in: (1) estrogen receptor positive (ER+) premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) ER+ postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative (ER-) patients with Stage II disease using one vs two years of combination chemotherapy; to compare the effect of adjuvant therapy in Stage II breast cancer using partial mastectomy and radiation vs modified radical or radical mastectomy; to compare the effect of the various adjunctive therapy programs upon survival patterns; and to correlate the estrogen receptor status with disease-free interval and survival.

**Technical Approach:** Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-FU, vincristine, and prednisone): (1) CMFVP for 1yr pre- or postmenopausal ER patients. (2) CMFVP for 2 yr pre- or postmenopausal ER patients. (3) CMFVP for 1 yr premenopausal ER+ patients. (4) Oophorectomy + CMFVP premenopausal ER+ patients. (5) Tamoxifen alone for 1 yr postmenopausal ER+ patients. (6) CMFVP for 1 yr postmenopausal ER+ patients. (7) Tamoxifen + CMFVP for 1 yr postmenopausal ER+ patients. Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

**Progress:** This study was closed to patient entry 15 Aug 89. Thirty-five patients were enrolled at MAMC. Twenty patients are still being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 81/064		<b>Status:</b> Terminated	
<b>Title:</b> SWOG 8027: The Natural History of Pathological Stage T(1-2) N(O), M(O) ER+ Breast Cancer					
<b>Start Date:</b> 03/20/81			<b>Est. Completion Date:</b> Jan 83		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> LTC Archie W. Brown, MC			COL Irwin B. Dabe, MC		
<b>Key Words:</b> Cancer:breast, natural history					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
				<b>Periodic Review:</b> 11/17/95	

**Study Objective:** To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative ( $T_{1-2} N_0 M_0$ ) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

**Technical Approach:** Patients having undergone radical, modified radical, or adequate local excision with node dissection for histologically proven breast carcinoma whose axillary nodes are negative for tumor and whose estrogen receptor status is positive are eligible. Patients undergoing local adequate excision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days post-operatively as outlined in the protocol. Only patients with pathologic Stage  $T_{1-2} N_0 M_0$  with a primary tumor of  $\leq 5$  cm are eligible. The primary tumor must be movable in relationship to the anterior chest wall and may not be involved with extensive skin ulcerations. This protocol involves no randomization or treatment. It consists only of follow-up and documentation of natural history. Patients will be stratified by primary tumor size,  $< 2$  cm by 2 to 5 cm, and by menopausal status. Patients will be followed until relapse or for 10 years, whichever comes sooner.

**Progress:** Closed to patient entry 1 Oct 82. Five patients were entered; three are still alive. This protocol was previously reported as completed; the protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients. SWOG has now terminated the protocol because it is felt that more data are unnecessary on the patients on this study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 84/018		<b>Status:</b> On-going
<b>Title:</b> SWOG 8216/38: Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer				
<b>Start Date:</b> 11/18/83			<b>Est. Completion Date:</b> Sep 85	
<b>Department:</b> SWOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b>			COL William D. Belville, MC	
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC	
MAJ Thomas M. Baker, MC			MAJ Alfred H. Chan, MC	
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC	
<b>Key Words:</b> cancer:bladder,BCG,adriamycin				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	11/17/95	

**Study Objective:** To compare the effectiveness of intravesical BCG immunotherapy with intravesical Adriamycin in chemotherapy with respect to disease-free interval and two-year recurrence rate; to compare the toxicity of topical immunotherapy and chemotherapy; and to obtain experience regarding disease-free interval and the recurrence rate in patients who develop tumor recurrence and are then crossed over to the alternative treatment arm.

**Technical Approach:** Following a standard transurethral resection, patients will be stratified by the presence or absence of documented carcinoma in situ and as to prior chemotherapy and then randomized to receive BCG immunotherapy or Adriamycin chemotherapy. Patients who develop tumor recurrence following treatment will be eligible for crossover to the other treatment arm.

**Progress:** This study was closed to patient entry 20 Dec 85. Three patients were enrolled at MAMC and are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 85/076		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II					
<b>Start Date:</b> 08/23/85			<b>Est. Completion Date:</b> Jun 87		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b> MAJ Michael D. Stone, MC MAJ Thomas M. Baker, MC			COL Irwin B. Dabe, MC CPT David R. Bryson, MC		
<b>Key Words:</b> Cancer:lung, small cell, radiation therapy, adriamycin, cis-platinum, cyclophosphamide, methotrexate, vincristine, VP-16					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		11/17/95	

**Study Objective:** To explore the response rate with the concurrent use of radiation therapy plus chemotherapy utilizing cis-platinum, VP-16, and vincristine in limited small cell carcinoma of the lung and to observe the toxicities of this combined modality program.

**Technical Approach:** Patients will be started on chemotherapy consisting of cis-platinum, VP-16, and vincristine and concurrent radiation therapy to the primary site. After completion of radiation therapy to the chest, prophylactic cranial radiation therapy will be given. After a brief rest period, the patients will be treated with 12 more weeks of conventional chemotherapy consisting of adriamycin, cytoxan, VP-16, vincristine, and methotrexate. Patients who show a complete response will be followed. Patients with less than a complete response will be taken off study and offered alternative therapy.

**Progress:** This study was closed to patient entry 19 March 86. It was previously reported as completed. In fact, two patients were entered and one is still being followed. The protocol was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 83/056	<b>Status:</b> On-going
<b>Title:</b> SWOG 8294: Evaluation of Adjuvant Therapy and Biological Parameters in Node Negative Operable Female Breast Cancer (ECOG, EST-1180), Intergroup Study		
<b>Start Date:</b> 03/18/83	<b>Est. Completion Date:</b> Feb 85	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> COL Friedrich H. Stutz, MC MAJ Timothy J. O'Rourke, MC MAJ Thomas M. Baker, MC		LTC James E. Congdon, MC COL Irwin B. Dabe, MC MAJ Alfred H. Chan, MC
<b>Key Words:</b> cancer:breast,surgery,biological parameters		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/89

**Study Objective:** To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whose pathological size is >3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

**Technical Approach:** Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cm in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

**Progress:** This study was closed to patient entry 15 May 88. Twelve patients were enrolled in previous years and nine continue to be followed. Three have expired.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 84/059		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III					
<b>Start Date:</b> 05/18/84			<b>Est. Completion Date:</b> May 86		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Friedrich H. Stutz, MC		
COL Irwin B. Dabe, MC			MAJ Thomas M. Baker, MC		
MAJ Timothy J. O'Rourke, MC			MAJ Michael D. Stone, MC		
<b>Key Words:</b> cancer:breast,chemotherapy,emergency room					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					11/17/95

**Study Objective:** To compare through a randomized prospective study the recurrence rates and disease-free intervals for postoperative axillary node positive estrogen receptor negative breast cancer patients given adjuvant therapy with either short term intense chemotherapy (FAC-M) or one year standard chemotherapy (CMFVP); to compare the effect of these two adjuvant therapies on survival; to compare the relative toxicity of the two therapies; to compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses; and to compare a multiple item questionnaire for assessing quality of life.

**Technical Approach:** Women who have histologically proven breast cancer with axillary lymph node metastasis and negative estrogen receptors will be entered 14-21 days post-lumpectomy or within 14-42 days post-mastectomy and randomly assigned to receive: Arm I a tapering course of oral prednisone for 6 weeks, weekly IV vincristine for 10 weeks, weekly IV methotrexate, and weekly IV 5-FU plus daily oral cyclophosphamide for a total of one year; or Arm II four cycles of adriamycin (IV day 1), cyclophosphamide (IV day 1), 5-FU (IV days 1 and 8), and methotrexate (IV day 22). Each cycle will be five weeks and total duration of therapy in this arm is approximately 20 weeks. Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy. Added to this protocol will be a sub-study to determine the prognostic significance of circulating human mammary epithelial antigens. This will involve blood tests prior to chemotherapy and then once every three months.

**Progress:** This study was closed to patient entry 15 Jun 90. Three patients were enrolled, 2 have died and 1 continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 85/009		<b>Status:</b> On-going
<b>Title:</b> SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II				
<b>Start Date:</b> 11/16/84			<b>Est. Completion Date:</b> Oct 86	
<b>Department:</b> SWOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b>			COL Friedrich H. Stutz, MC	
COL Irwin B. Dabe, MC			MAJ Timothy J. O'Rourke, MC	
MAJ Michael D. Stone, MC			CPT David R. Bryson, MC	
MAJ Thomas M. Baker, MC				
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, m-BACOD				
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	11/17/95

**Study Objective:** To determine an approximate complete remission rate and remission duration for the treatment program of cyclophosphamide, doxorubicin, vincristine, dexamethasone, and bleomycin with intervening moderate dose of methotrexate and leucovorin rescue (m-BACOD) in patients with intermediate and high grade non-Hodgkin's lymphoma and to assess the feasibility of using this regimen in the SWOG with the intent of using m-BACOD in a future Phase III trial.

**Technical Approach:** Patients will be stratified according to marrow reserve status and creatinine clearance. Treatment will consist of ten 3-week courses. Cytosan, adriamycin, vincristine, and bleomycin will be given IV on day 1. Dexamethasone will be given by mouth daily for 5 days, and methotrexate will be given on days 8 and 15 at 200 mg/m<sup>2</sup>. Leucovorin will be given 10 mg/m<sup>2</sup> by mouth after each methotrexate injection every 6 hours for eight doses. An adequate trial will be defined as the completion of two complete cycles of m-BACOD. Patients with documented progressive disease or less than complete response after an adequate trial will be taken off study. Those with complete response will continue on study with no further chemotherapy.

**Progress:** This study was closed to patient entry 26 April 1985 and reported as completed. However, two patients had been enrolled in the study and are still being followed. The study was reactivated in December 1993 so that SWOG could continue to collect data on these patients.

### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol no.:** 86/007      **Status:** On-going

**Title:** SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Phase III

**Start Date:** 10/18/85      **Est. Completion Date:** Sep 87

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ Paul C. Sowray, MC

<b>Associate Investigators:</b>	COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC	LTC Howard Davidson, MC
MAJ Thomas M. Baker, MC	MAJ Michael D. Stone, MC
CPT David R. Bryson, MC	

**Key Words:** leukemia:lymphoblastic,consolidation regimens

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	<b>OMA Cost:</b>	
\$0	\$0.00	11/17/95

**Study Objective:** To compare the effects on remission duration and survival of two consolidation regimens: the L-10-M consolidation used in SWOG 8001 versus a regimen employing daunomycin, cytosine, arabinoside, 6-thioguanine and escalating methotrexate/Lasparaginase in patients with adult lymphoblastic leukemia and to compare the toxicities of the two consolidation regimens.

**Technical Approach:** Patients will begin remission induction with vincristine, prednisone, adriamycin, methotrexate, cyclophosphamide, and adriamycin (36 days), followed by a 14 day rest period. On day 30, patients will have an Ommaya reservoir placed in the frontotemporal area of the skull. Patients failing to achieve an A1 marrow status on induction therapy will go off study. Patients with complete remission will be randomized to one of the following consolidation regimens: ARM I (L-10-M) methotrexate and Ara-c, daily x 5 on days 1, 36, and 71; Ara-c and 6-thioguanine every 12 hr for 12 doses on days 15, 50, and 85; methotrexate days 15, 17, 57, and 59; vincristine and prednisone days 50 and 57; L-asparaginase beginning day 99, three times weekly for a total of 6 doses, and cyclophosphamide day 110 following last dose of L-asparaginase. Arm II: daunomycin days 1-3, Ara-C continuous infusion days 1-5, 6-thioguanine every 12 hr days 15, followed by a 21-28 day rest period. Methotrexate every 10 days from 28-98, L-asparaginase every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 weeks for 36 months or until relapse. An adequate trial will be the completion of remission induction.

**Progress:** This study closed to patient entry 15 Nov 91. Seven patients were enrolled MAMC. All original patients enrolled at MAMC have died but 1 patient has transferred in (previous FY) and is being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/033		<b>Status:</b> Terminated	
<b>Title:</b> SWOG 8501 (INT 0051): Intraperitoneal Cis-platinum/IV Cyclophosphamide vs IV cis-platinum/IV Cyclophosphamide in Patients with Non-measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III ...					
<b>Start Date:</b> 01/16/87			<b>Est. Completion Date:</b> Indefinite		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Thomas M. Baker, MC		
COL Irwin B. Dabe, MC			LTC Lauren K. Colman, MC		
MAJ David M. Dunning, MC			MAJ Ruben D. Sierra, MC		
CPT David R. Bryson, MC			COL Roger B. Lee, MC		
<b>Key Words:</b> cancer:ovarian, chemotherapy, IP, IV cyclophosphamide, cisplatin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		11/17/95	

**Study Objective:** To perform a Phase III randomized trial of intermediate dose intraperitoneal (IP) cis-platinum and intravenous (IV) cyclophosphamide vs intermediate dose IV cis-platinum and cyclophosphamide for optimal Stage III ovarian cancer; to evaluate the comparative toxicities of the two regimens; and to determine, in the setting of a prospective randomized trial, if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and IP drug administration.

**Technical Approach:** Only patients with epithelial neoplasms will be eligible. Patients will be stratified by amount of residual disease and performance. They will be randomized to Arm I or Arm II. Arm I: IV cisplatin, 100 mg/m<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup> every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m<sup>2</sup> plus IV cyclophosphamide, 600 mg/m<sup>2</sup>, every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

**Progress:** This study was closed to patient entry 15 Jul 92. One patient was entered in Dec 86 and refused second look surgery so he was taken off the protocol, and is still alive. The protocol was terminated by SWOG because it was felt that more data on the subjects on this study were not necessary.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/107		<b>Status:</b> On-going
<b>Title:</b> SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III				
<b>Start Date:</b> 08/21/87			<b>Est. Completion Date:</b> Aug 90	
<b>Department:</b> SWOG			<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC	
COL William D. Belville, MC			COL Victor J. Kiesling, MC	
LTC Lauren K. Colman, MC			MAJ Thomas M. Baker, MC	
MAJ David M. Dunning, MC			MAJ Ruben D. Sierra, MC	
CPT Denis Bouvier, MC				
<b>Key Words:</b> cancer:bladder,BCG,immunotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>	
\$0		\$0.00	11/17/95	

**Study Objective:** To compare the effectiveness of intravesical and percutaneous BCG immunotherapy given on a maintenance versus no maintenance schedule with respect to disease-free interval and rate of tumor recurrence in patients with transitional cell carcinoma of the bladder; to assess the toxicity of maintenance and no maintenance BCG immunotherapy; and to assess the association of intermediate strength PPD skin test reactivity with disease free status in patients treated with BCG immunotherapy.

**Technical Approach:** Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG administration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenance or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study.

**Progress:** This study closed to patient entry 15 Dec 88. Eleven patients were entered in the study and 10 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 86/080		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 08/15/86			<b>Est. Completion Date:</b> Jul 89		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Thomas M. Baker, MC		
COL Irwin B. Dabe, MC			LTC Lauren K. Colman, MC		
MAJ David M. Dunning, MC			CPT David R. Bryson, MC		
<b>Key Words:</b> lymphoma:non-Hodgkin's,chemotherapy,CHOP,m-BACOD,M					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		11/17/95	
\$0		\$0.00			

**Study Objective:** To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

**Technical Approach:** Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycles): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV) and prednisone (PO). Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV), bleomycin (IV), dexamethasone (PO), methotrexate (IV), and calcium Leucovorin rescue after each MTX dose. Arm III (Pro-MACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide (IV), doxorubicin (IV), VP-16 (IV), Prednisone(PO), Ara-C (IV), bleomycin (IV), vincristine (IV), methotrexate (IV), calcium leucovorin rescue after each MTX dose, and trimetheprim-sulfamethoxazole (PO). Arm IV (MACOP-B will be given over 12 weeks): methotrexate (IV), calcium leucovorin rescue after each MTX bolus, doxorubicin (IV), cyclophosphamide (IV), vincristine (IV), bleomycin (IV), prednisone (PO), and trimethoprimsulfa (PO). Patients with documented progressive disease may be taken off study at any time; however patients will preferably be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

**Progress:** This study was closed to patient entry 15 June 1991, and was previously reported as completed. However, two patients were transferred in to MAMC from another Army medical center so it was reactivated in Dec 93. MAMC now follows these patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 85/073	<b>Status:</b> On-going
<b>Title:</b> SWOG 8590: Phase III Study to Determine the Effect of Combining Chemotherapy with Surgery and Radiotherapy for Resectable Squamous Cell Carcinoma of the Head and Neck, Phase III (Intergroup Group.....		
<b>Start Date:</b> 06/28/85	<b>Est. Completion Date:</b> May 87	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
COL William J. Gernon, MC	COL Irwin B. Dabe, MC	
MAJ Michael D. Stone, MC	MAJ Timothy J. O'Rourke, MC	
LTC Donald B. Blakeslee, MC	CPT David R. Bryson, MC	
<b>Key Words:</b> head & neck,surgery,chemotherapy,radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

**Technical Approach:** After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cisplatinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

**Progress:** This study was closed to patient entry 1 Feb 90. Three patients were entered in previous years and are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 85/064		<b>Status:</b> Terminated	
<b>Title:</b> SWOG[ 8591colon] NCI Intergroup #0035, An Evaluation of Levamisole Alone or Levamisole plus 5-Fluorouracil as Surgical Adjuvant Treatment for Resectable Adenocarcinoma of the Colon, Phase III - Intergroup					
<b>Start Date:</b> 05/24/85			<b>Est. Completion Date:</b> Apr 87		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Thomas M. Baker, MC		
COL Friedrich H. Stutz, MC			COL Irwin B. Dabe, MC		
MAJ Jens A. Strand, MC			MAJ Timothy J. O'Rourke, MC		
MAJ Michael D. Stone, MC			CPT David R. Bryson, MC		
<b>Key Words:</b> cancer:colon,levamisole,5-Fluorouracil					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		11/17/95
			\$0.00		

**Study Objective:** To assess the effectiveness of levamisole alone and levamisole plus 5-FU as surgical adjuvant regimens for resectable colon cancer; to compare each regimen to untreated controls to determine whether it yields improved survival and if it yields improved time to recurrence, with evaluations conducted independently in patients with Dukes stage B and Dukes stage C lesions.

**Technical Approach:** Patients with adenocarcinoma arising in the colon who have had a potentially curative section will be eligible. The patients with modified Dukes B2 (serosal penetration) or B3 (invasion of adjacent organs by direct extension) will be randomized to either follow-up without adjuvant therapy or adjuvant therapy with levamisole plus 5-FU. Patients with modified Dukes Stage C (involvement of regional lymph nodes) will be randomized to follow-up without adjuvant therapy, adjuvant therapy with levamisole alone, or adjuvant therapy with levamisole plus 5-FU.

**Progress:** This study was closed to patient entry 21 Oct 87. Seven patients were enrolled in previous years and 6 are still living. The protocol has been terminated by SWOG because it was felt all they had collected all of the data that would be beneficial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 87/045		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-lymphocytic Leukemia					
<b>Start Date:</b> 02/27/87			<b>Est. Completion Date:</b> Feb 90		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
LTC Lauren K. Colman, MC			LTC Howard Davidson, MC		
MAJ Thomas M. Baker, MC			MAJ David M. Dunning, MC		
MAJ Ruben D. Sierra, MC			CPT David R. Bryson, MC		
<b>Key Words:</b> leukemia:non-lymphocytic,Ara-C,daunorubicin,cytosine arabinoside					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>02/21/97</b>

**Study Objective:** To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high-dose cytosine arabinoside and daunorubicin; to compare the duration of complete remission and of disease-free survival among patients who receive one of the three combinations of induction and consolidation regimens listed below; to determine the comparative toxicities of these three programs, and to determine the feasibility of implementing a predetermined approach to supportive care for these patients in a multi-institutional cooperative group setting.

**Technical Approach:** Patients will be stratified according to age and institution. Induction therapy will consist of standard dose Ara-C plus daunorubicin (Arm I) or high dose Ara-C + daunorubicin (Arm II). Patients requiring a second cycle of induction will receive the same doses as cycle 1, following the recovery of hematologic toxicities. Consolidation chemotherapy will begin when bone marrow and blood counts have recovered or on day 28 after the last induction cycle. Patients initially randomized to Arm I will be randomized to Arm III (high dose, one cycle only) or Arm IV (standard dose, two cycles). Patients initially randomized to Arm II (high dose) will be assigned to Arm III. Following the completion of consolidation, no further therapy will be given and patients will be followed only. Supportive care will include a predetermined antibiotic regimen determined by the physician.

**Progress:** This study was closed to patient entry 1 Dec 91. Of the seven patients enrolled at MAMC, 5 have died and 2 are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 90/039		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8710: Trial of Cytectomy Alone Versus Neoadjuvant M-VAC + Cytectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877, CALGB-8891)					
<b>Start Date:</b> 02/16/90			<b>Est. Completion Date:</b> Mar 92		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Rodney C. Davis, MC					
<b>Associate Investigators:</b>					
MAJ Paul C. Sowray, MC			LTC Howard Davidson, MC		
MAJ Everardo E. Cobos Jr., MC			MAJ Mark H. Kozakowski, MC		
CPT Denis Bouvier, MC			MAJ Patrick L. Gomez, MC		
LTC Robert L. Sheffler, MC			LTC Kenneth A. Bertram, MC		
			LTC John A. Vaccaro, MC		
<b>Key Words:</b> cancer:bladder,cystectomy,M-VAC					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		02/21/97	

**Study Objective:** To study insulin induced hypoglycemia as a model of acute stress and to determine if the change in testosterone seen with acute stress is related to cortisol alone or whether it can also be seen with the stimulation of other adrenal precursor products.

**Technical Approach:** Ten healthy male volunteers (18-35 years) who are without evidence of current acute or chronic illness will have an insulin tolerance test done with blood samples drawn for cortisol, testosterone, immunoactive LH, bioactive LH, estradiol, and glucose, every 15 minutes for one hour prior to the human insulin bolus to establish baseline values. Blood samples will continue to be drawn every 15 minutes for 180 minutes after injection of the insulin. SHBG will be measured on the first and last sample and endorphin levels will be measured at baseline and at times corresponding to maximal hypoglycemia. A standard multiple dose metyrapone test will be performed one month from the insulin tolerance test. Just before the first dose and four hours after the last dose, serum samples will be obtained for cortisol, estradiol, immunoactive LH, bioactive LH, testosterone, ACTH, SHBG, endorphins, and 11-deoxycortisol. The relationship of bioactive LH to immunoactive LH will be compared using the biologic to immunologic ratio both before and during the acute stress. The data from the metyrapone test will be used to determine if metyrapone can cause a decrease in serum testosterone acutely. Again, the B/I ratio will be compared pre and post-test. Changes in serum concentrations of the measured hormones will be analyzed by repeated measures analysis of variance.

**Progress:** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 88/065		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation Therapy					
<b>Start Date:</b> 07/15/88			<b>Est. Completion Date:</b> Jun 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>					
CPT Denis Bouvier, MC		COL Irwin B. Dabe, MC			
MAJ Rahul N. Dewan, MC		LTC Steven S. Wilson, MC			
<b>Key Words:</b> lymphoma:non-Hodgkin's,radiotherapy,CHOP,chemotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	11/17/95	

**Study Objective:** To evaluate, in a cooperative group setting, the difference in survival, time to treatment failure, and toxicity of two curative approaches to the treatment of patients with localized, intermediate or high grade non-Hodgkin's lymphoma.

**Technical Approach:** All patients must have biopsy proven non Hodgkin's lymphoma of intermediate or high grade histology except lymphoblastic lymphoma. Patients must have had all visible tumor removed (excisional biopsy) and must have clinically adequate liver and myocardial function to begin treatment at full doses. Patients with known central nervous system disease, previous cancer with a possibility for recurrence which might affect survival or prior chemo or radiotherapy will be ineligible. All patients will be stratified at the time of initial registration by the following: (1) age (<65 years vs >65 years); (2) Stage (I or Ie vs nonbulky II or IIE); (3) histology (diffuse large cell vs other); (4) location of disease (GI involved vs non-GI, abdominal vs non-GI, other); (5) all disease resected vs residual measurable disease. Patients will be randomized to CHOP\* (Arm I) or to CHOP plus radiation therapy (Arm II). A complete course of chemotherapy on Arm I will consist of the administration of CHOP every 21 days for eight consecutive cycles unless progressive disease develops. A complete course of chemotherapy for Arm II will consist of the administration of CHOP every 21 days for three consecutive cycles unless progressive disease develops. Radiation therapy will begin immediately after the third cycle of CHOP. Radiation therapy dose, duration, and treatment volume will be determined jointly by the radiation oncologist and the medical oncologist. All patients will be followed at three month intervals until death. CHOP: Cyclophosphamide, 750 mg/m<sup>2</sup> IV, day 1; Doxorubicin, 50 mg/m<sup>2</sup> IV, day 1; Vincristine, 1.4 mg/m<sup>2</sup> IV, day 1; Prednisone, 100 mg/day po, days 1-5.

**Progress:** This study closed to patient entry 15 June 95. Nine patients have been enrolled at MAMC. Two have expired, so seven continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 88/076		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8738: Treatment of Extensive Non-small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III					
<b>Start Date:</b> 09/16/88			<b>Est. Completion Date:</b> Sep 91		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Mark H. Kozakowski, MC			CPT Denis Bouvier, MC		
LTC Kenneth A. Bertram, MC					
<b>Key Words:</b> cancer:lung:non-small cell,cisplatin,mitomycin-C					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		11/17/95

**Study Objective:** To compare standard dose cisplatin chemotherapy to high dose cisplatin in hypertonic saline alone to high dose cisplatin/mitomycin-C in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; and to compare the relative toxicities of these three chemotherapy regimens in patients with extensive non-small cell lung cancer.

**Technical Approach:** Patients will be randomized to one of the following arms: Arm I: standard dose cisplatin (50 mg/m<sup>2</sup>, IV) every four weeks for a maximum of eight cycles; ARM II: high dose cisplatin alone (100 mg/m<sup>2</sup>, IV) every four weeks for a maximum of four cycles; ARM III: high dose cisplatin (100 mg/m<sup>2</sup> IV) plus mitomycin-C (8 mg/m<sup>2</sup> IV) given every four weeks for a maximum of four cycles. All patients will have an initial assessment of response after two cycles and then reassessment after four cycles of therapy. Patients on Arm I who respond to treatment may receive continued therapy to a maximum of eight cycles. Upon progression of disease, unacceptable toxicity, or patient request, patients will be taken off treatment. All patients will be followed until death.

**Progress:** This study was closed to patient entry 1 Jun 90. Six patients were enrolled at MAMC in previous years and 1 continues to be followed.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 90/063		<b>Status:</b> Terminated	
<b>Title:</b> SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients With Advanced Germ Cell Tumors					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Apr 93		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>					
MAJ Mark H. Kozakowski, MC		LTC Howard Davidson, MC			
MAJ Patrick L. Gomez, MC		MAJ Everardo E. Cobos Jr., MC			
LTC Kenneth A. Bertram, MC		CPT Denis Bouvier, MC			
		LTC Robert L. Sheffler, MC			
<b>Key Words:</b> tumor:germ cell,etoposide,cisplatin,carboplatin,CBDCA					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		11/17/95	

**Study Objective:** To determine in a randomized trial the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens; etoposide + cisplatin and etoposide + carboplatin, for good risk patients with germ cell tumors.

**Technical Approach:** Patients with active advanced Stage II or Stage III testicular nonseminomatous germ cell tumor with a probability of complete response of >0.5 will be eligible. Patients will be randomized to Treatment Arm A (carboplatin + etoposide, given every 28 days for four cycles) or Treatment Arm B (cisplatin + etoposide every 21 days for four cycles). Following completion of chemotherapy, a complete assessment of all sites of disease will be performed. Following completion of four cycles of chemotherapy and radiographic and marker assessment, surgical resection of all residual masses will be done if deemed necessary by the principal investigator. If no residual malignant tumor or only mature teratoma is completely resected at surgery, no further therapy will be administered. If residual malignant tumor is found but is completely excised, then two more cycles of treatment will be administered. If residual malignant tumor is found but is unresectable, then the patient will receive additional therapy with standard GCT regimens or other therapy as may be indicated at the discretion of the treating physician.

**Progress:** This study closed to patient entry 15 Dec 90. One patient was enrolled at MAMC and is still being followed. This study was terminated by SWOG as it was determined that no further data collection was necessary on the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 94/119	<b>Status:</b> On-going
<b>Title:</b> SWOG 8794: Treatment of Pathologic Stage C Carcinoma of the Prostate With Adjuvant Radiotherapy		
<b>Start Date:</b> 06/03/94	<b>Est. Completion Date:</b> Jun 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC		
<b>Associate Investigators:</b>		
COL John C. Norbeck, MC	COL John N. Wettlaufer, MC	
CPT Timothy O. Taylor, MC	LTC Kurt L. Hansberry, MC	
CPT Bradley F. Schwartz, MC	CPT Michael D. Bagg, MC	
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
	MAJ Timothy P. Rearden, MC	
<b>Key Words:</b> Cancer:prostate, radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** 1) To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3N0M0) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. 2) To assess the qualitative and quantitative toxicities of patients with pathologic Stage C (T3N0M0) carcinoma of the prostate when treated with external beam radiotherapy.

**Technical Approach:** Patients who have undergone radical prostatectomy and pelvic lymphadenectomy for clinical Stage A or B disease with a histologically proven diagnosis of pathologic Stage C (T3N0M0) carcinoma of the prostate will be randomized to receive either postoperative adjuvant radiation therapy (ARM I) or no adjuvant therapy (ARM II). The studies primary objective is to determine whether adjuvant radiation therapy has an effect on local control of the cancer and cancer-specific survival.

**Progress:** This study was closed to patient entry, 1 Jan 97. One patient was enrolled at MAMC and continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 88/066		<b>Status:</b> On-going
<b>Title:</b> SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)				
<b>Start Date:</b> 07/15/88		<b>Est. Completion Date:</b> Jun 91		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> CPT Denis Bouvier, MC		COL Irwin B. Dabe, MC		
<b>Key Words:</b> Hodgkin's Disease,chemotherapy				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		11/17/95

**Study Objective:** To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP---->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

**Technical Approach:** Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study. MOPP: Nitrogen mustard, 6 mg/m<sup>2</sup> IV, days 1 and 8, Vincristine, 1.4 mg/m<sup>2</sup> IV, days 1 and 8, Procarbazine, 100 mg/m<sup>2</sup> PO per day x 14 days, Prednisone 40 mg/m<sup>2</sup> PO per day x 14 days. ABVD: Adriamycin, 25 mg/m<sup>2</sup> IV, days 1 and 15, Bleomycin, 10 units/m<sup>2</sup> IV, days 1 and 15, Vinblastine, 6 mg/m<sup>2</sup> IV days 1 and 15, DTIC, 375 mg/m<sup>2</sup> IV, days 1 and 15. The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/m<sup>2</sup> IV, day 8; bleomycin, 10 units/m<sup>2</sup> IV day 8; and vinblastine, 6 mg/m<sup>2</sup> IV, day 8.

**Progress:** This study was closed to patient entry 1 Aug 89. One patient was enrolled at MAMC (FY88) and is still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 90/064		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas					
<b>Start Date:</b> 04/20/90			<b>Est. Completion Date:</b> Apr 94		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
MAJ Patrick L. Gomez, MC			CPT Denis Bouvier, MC		
LTC Kenneth A. Bertram, MC			LTC Robert L. Sheffler, MC		
<b>Key Words:</b> lymphoma,alpha-interferon,ProMACE-Mopp,chemo					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		11/17/95
			\$0.00		

**Study Objective:** To compare the disease-free survival of patients with low grade malignant lymphoma who receive alpha-interferon consolidation therapy after intensive induction with chemotherapy, with or without radiation therapy, to those who receive induction therapy alone; to determine the complete response rate, response duration, and survival of low grade lymphoma patients treated with ProMACE-MOPP; and to compare the toxicities of induction and induction plus consolidation therapy in this patient population.

**Technical Approach:** Patients must have biopsy proven, measurable, Stage III or IV non-Hodgkin's lymphoma of low grade histology. Patients will receive 6 cycles of induction chemotherapy (ProMACEMOPP, days 1-8) unless progressive disease develops during this treatment. At the completion of induction therapy, patients will be restaged to assess response. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete radiographic and laboratory evaluation for evidence of persistent lymphoma approximately one month after completion of chemotherapy. If no evidence of disease is found these patients will be randomized to Alpha IFN or observation. Patients in partial response and whose bone marrow remains positive after 6 cycles of induction chemotherapy will receive 2 additional cycles of chemotherapy and then be reevaluated. If the bone marrow remains involved or the patient has less than a partial response after a total of 8 cycles, the patient will be removed from further protocol therapy. If after 8 cycles, the bone marrow is negative and the patient is in partial response, the patient will receive radiotherapy. Complete responders after induction chemotherapy; complete responders after induction chemotherapy plus radiation therapy; and partial responders after chemotherapy plus radiation therapy will be randomized to consolidation alpha interferon or observation, approximately one month after completion of therapy.

**Progress:** This study was closed to patient entry 15 Nov 94. Four patients have been entered at MAMC. All patients are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 89/080		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast....					
<b>Start Date:</b> 09/15/89			<b>Est. Completion Date:</b> Sep 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			MAJ Paul C. Sowray, MC		
MAJ Mark H. Kozakowski, MC			MAJ Everardo E. Cobos Jr., MC		
MAJ Patrick L. Gomez, MC			CPT Denis Bouvier, MC		
LTC Kenneth A. Bertram, MC			LTC Robert L. Sheffler, MC		
<b>Key Words:</b> cancer:breast,chemoendocrine therapy,CAF,tamoxifen					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		11/17/95
			\$8692.00		

**Study Objective:** To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

**Technical Approach:** Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

**Progress:** This study closed to patient entry 1 Aug 95. Seven patients have been entered in this study at MAMC. One patient expired in FY 96, 6 others are still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 91/020	<b>Status:</b> Terminated
<b>Title:</b> SWOG 8816: Study of 13-cis Retinoic Acid (Accutane) Plus Interferon-A (Roferon-A) in Mycosis Fungoides, Phase II		
<b>Start Date:</b> 12/07/90	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	MAJ William A. Phillips	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
LTC Robert L. Sheffler, MC	LTC Kenneth A. Bertram, MC	
CPT Jennifer L. Cadiz, MC	LTC Robert B. Ellis, MC	
<b>Key Words:</b> mycosis fungoides,retinoic acid,interferon-A		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To evaluate the response rate of mycosis fungoides treated with the drug combination of 13-cis retinoic acid (Accutane) plus alpha interferon (Roferon-A) and to assess the qualitative and quantitative toxicities of the regimen in a phase II study.

**Technical Approach:** Mycosis fungoides is an uncommon lymphoma manifesting initially with skin presentation, but the disease is felt to be incurable. The regimen will be 13-cis retinoic acid, 1.0 mg/kg/day, po in two divided doses (plus vitamin E, 400 IU/day) and alpha interferon,  $3 \times 10^6$  microgm/m<sup>2</sup> subcutaneously, three times per week. After eight weeks of treatment, patients with progressive disease will go off treatment. Patients with stable disease or partial or complete remission will be treated for eight more weeks. At this point, patients who have not demonstrated a partial response will be taken off study. Patients who have partial or complete response will be treated for an additional one (complete response) or two years (partial response).

**Progress:** This study closed to patient entry 3 Jan 93. One patient was enrolled in FY92 and is still alive. This study has been terminated by SWOG because it was felt they had collected all the data that would be beneficial to the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/087		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8819: Central Lymphoma Repository Tissue Procurement Protocol; Companion Protocol to SWOG Studies: 8516, 8736, 8809, 8907, and 8954					
<b>Start Date:</b> 08/02/91			<b>Est. Completion Date:</b> Aug 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			MAJ Patrick L. Gomez, MC		
MAJ Everardo E. Cobos Jr., MC			LTC Robert L. Sheffler, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
CPT Jennifer L. Cadiz, MC			MAJ James S. D. Hu, MC		
LTC Kenneth A. Bertram, MC					
<b>Key Words:</b> lymphoma:tissue procurement					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objective:** To acquire fresh snap-frozen lymphoma tissue to establish a central lymphoma tissue repository; to establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group; to use repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status; and to determine if pretreatment phenotype or genotype predict patient outcome with respect to complete response rate, time to progression, and survival using prospective trial designs.

**Technical Approach:** Patients will be treated according to guidelines outlined in the specific SWOG studies. Treatment decisions will not be based on findings of the Central Lymphoma Laboratory, although clinical variables will be correlated with laboratory findings. The tissue samples will be taken from the pretreatment diagnostic biopsy or rebiopsy based on clinical decisions. Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (hematoxylin and eosin) histologic section with accompanying pathology report. The H&E stained slide and report will accommodate morphologic correlation with immunologic findings. Tissue section analysis will be performed at the University of Arizona using three stage immunohistochemistry. Future molecular studies entailing hybridization studies of RNA and DNA fragments using DNA probes will be performed as outlined in future protocols.

**Progress:** This is a companion study using tissue from other SWOG protocols. Tissue has been collected on three patients.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 90/027	<b>Status:</b> On-going
<b>Title:</b> SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary....		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Dec 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC		MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC		CPT Denis Bouvier, MC
LTC Kenneth A. Bertram, MC		LTC Robert L. Sheffler, MC
<b>Key Words:</b> cancer:breast,chemotherapy,chemohormonal therapy,premenopausal		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$8200.00	02/21/97

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** This study closed to patient entry 1 Feb 94. Six patients have been enrolled at MAMC in previous years. One patient has been lost to follow-up, five are still being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 90/047		<b>Status:</b> On-going
<b>Title:</b> SWOG 8854: prognostic Value of Cytometry Measurements of Breast Cancer DNA from Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814				
<b>Start Date:</b> 03/16/90		<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> cancer:breast,DNA,cytometry,postmenopausal				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		11/17/95

**Study Objective:** To determine if ploidy analysis of breast cancer by routine clinical flow cytometry (CFM) technique can predict response to therapy and survival of patients registered to SWOG 8814 and to determine if ploidy analysis by image processing technique more accurately predicts patient response to therapy and survival than ploidy analysis by flow cytometry.

**Technical Approach:** Two paraffin blocks, one representing the highest grade region of the primary tumor, the second representing the highest grade regional metastasis in a positive lymph node, will be used. From each of these blocks, two to five sections will be cut and a nuclear suspension prepared. From each suspension, a cytospin preparation will be prepared and stained with Dif-Quik to ensure that the cells present in the H & E slide are represented adequately in the nuclear preparation. A second cytospin preparation will be prepared for staining by the Feulgen technique for image processing DNA analysis. The remainder of the nuclear preparation will be stained with propidium iodide following RNase digestion for FCM DNA analysis. Cox regression modeling will be used to explore the prognostic value of ploidy status as determined by FCM and by image processing, in conjunction with the covariates tumor size, age, ER and PgR levels, and number of nodes.

**Progress:** This study closed to patient entry 15 Feb 95. This is a companion study using tissue from SWOG 8814. Six samples have been studied, one of the patients has expired.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/067		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8855: Prognostic Value of Cytometry Measurements of Cellular DNA Parameters in Locally Advanced, Previously Untreated Head and Neck Cancer Patients					
<b>Start Date:</b> 06/14/91			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
<u>Progress:</u> Four patients have been entered into this study at MAM MAJ			MAJ Everardo E. Cobos Jr., MC		
Paul C. Sowray, MC			LTC Robert B. Ellis, MC		
LTC Robert L. Sheffler, MC					
CPT Jennifer L. Cadiz, MC					
<b>Key Words:</b> cancer:head & neck,cytometry,DNA					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b> 11/17/95	

**Study Objective:** To evaluate the prognostic value of cellular DNA parameters of degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) in predicting treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck treated initially with cytotoxic therapy and to assess the correlation of DNA index and SPF with other patient clinical characteristics.

**Technical Approach:** Squamous cell cancers of the head and neck display a high degree of responsiveness to chemotherapy and/or radiotherapy, but a significant minority are exquisitely resistant to these treatment modalities. This will be a companion study to all SWOG head and neck cancer protocols utilizing chemotherapy as initial treatment and will use the patients registered on those studies. This study will use flow cytometrically determined cellular parameters, particularly cellular DNA content, to help identify prognostic outcome in this group of tumors. Specimens will be obtained at the time of biopsy for diagnosis, at completion of therapy if the tumor persists, or if a biopsy is performed to confirm a clinical complete response or document recurrence. All resected specimens will be sent for flow cytometry analysis. The degree of DNA aneuploidy (DNA index) and proliferative activity (SPF) will be determined by flow cytometry. These measurements will be correlated with the clinical characteristics of the patient at the time of biopsy to help predict treatment response, time to treatment failure, and survival in patients with squamous cell carcinoma of the head and neck.

**Progress:** Four patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 90/055	<b>Status:</b> On-going
<b>Title:</b> SWOG 8892 (EST 2388, RTOG 8817, INT 0099): A Study of Radiotherapy with or without Concurrent Cisplatin in Patients with Nasopharyngeal Cancer, Phase III		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Mark H. Kozakowski, MC	
LTC Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
MAJ Michael R. Morris, MC	LTC Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:nasopharyngeal,5-Fluorouracil,cisplatin,radiotherapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$3900.00	11/17/95

**Study Objective:** To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

**Technical Approach:** Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

**Progress:** This study was closed to patient entry 1 Feb 93. Nine patients were enrolled in previous years, one expired in FY 96 and the other eight are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 90/029	<b>Status:</b> On-going
<b>Title:</b> SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History...		
<b>Start Date:</b> 01/19/90	<b>Est. Completion Date:</b> Jan 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Mark H. Kozakowski, MC	MAJ Paul C. Sowray, MC	
MAJ Patrick L. Gomez, MC	MAJ Everardo E. Cobos Jr., MC	
LTC Kenneth A. Bertram, MC	CPT Denis Bouvier, MC	
	LTC Robert L. Sheffler, MC	
<b>Key Words:</b> cancer:breast,chemotherapy,endocrine therapy		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$5000.00	02/21/97

**Study Objective:** To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

**Technical Approach:** Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

**Progress:** This study was closed to patient entry 1 Feb 93. Nine patients were enrolled in previous years, one expired in FY 97 and the other seven are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 89/021		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin = 5-FU, High-Dose Leucovorin + 5-FU, Levamisole + 5-FU, or Low-Dose Leucovorin + 5-FU + Levamisole Following Curative Resection in...					
<b>Start Date:</b> 02/17/89			<b>Est. Completion Date:</b> Feb 92		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			COL Irwin B. Dabe, MC		
MAJ Mark H. Kozakowski, MC			CPT Denis Bouvier, MC		
LTC Kenneth A. Bertram, MC			MAJ Everardo E. Cobos Jr., MC		
<b>Key Words:</b> cancer:colon,resection,chemotherapy,leucovorin,levamisole					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		02/21/97
			\$50.00		

**Study Objective:** To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

**Technical Approach:** Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/ mesenteric implants resected enbloc (yes/no); and obstruction (yes/no). RANDOMIZE TO: (1) Observation; (2) Leucovorin 20 mg/m<sup>2</sup> + 5-FU 425 mg/m<sup>2</sup>; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses; (3) Leucovorin 500 mg/m<sup>2</sup> + 5-FU 600 mg/m<sup>2</sup>; Leucovorin by IV 2 hour infusion, 5-FU IV push beginning 1 hr after start of Leucovorin infusion, repeated weekly for 6 wks, followed by a 2-wk rest period, each 8-wk cycle (1 course) will be repeated for 4 courses. Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole).

**Progress:** Eighteen patients were enrolled at MAMC prior to closure to patient entry on 30 Jul 92. One patient was lost to follow-up, five patients have died from their disease and 12 continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 91/089	<b>Status:</b> On-going
<b>Title:</b> SWOG 8947: Central Lymphoma Serum Repository Protocol; Companion Protocol to SWOG Studies 8516, 8736, 8809, and 8816		
<b>Start Date:</b> 08/02/91	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Luke M. Stapleton, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	LTC Howard Davidson, MC	
MAJ Everardo E. Cobos Jr., MC	MAJ Patrick L. Gomez, MC	
LTC Robert B. Ellis, MC	LTC Robert L. Sheffler, MC	
CPT Jennifer L. Cadiz, MC	MAJ Richard C. Tenglin, MC	
LTC Kenneth A. Bertram, MC	MAJ James S. D. Hu, MC	
<b>Key Words:</b> lymphoma:serum repository		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To establish a central lymphoma serum repository that will serve as a resource to provide specimens for current and future scientific studies and to utilize the Southwest Oncology Group clinical data base to perform clinicopathologic correlations with the results of those studies.

**Technical Approach:** No therapy will be utilized in this study and patient treatment will not be based on this study. Patients must meet the eligibility criteria and be registered to one of the following SWOG protocols: 8516, 8809, 8736, or 8816. Ten cc's of blood will be drawn prior to protocol treatment and shipped to the SWOG Lymphoma Serum Repository at Loyola University Medical School.

**Progress:** This is a companion protocol to other SWOG studies. Two specimens have been collected in previous years .

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/007		<b>Status:</b> On-going	
<b>Title:</b> SWOG 8957: Feasibility Trial of Post-Operative Radiotherapy Plus Cisplatin Followed by Three Courses of 5-FU Plus Cisplatin in Patients with Resected Head and Neck Cancer, Phase II Pilot					
<b>Start Date:</b> 10/19/90			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Paul C. Sowray, MC			MAJ William A. Phillips		
LTC Luke M. Stapleton, MC			MAJ Everardo E. Cobos Jr., MC		
LTC Robert L. Sheffler, MC			LTC Robert B. Ellis, MC		
CPT Jennifer L. Cadiz, MC					
<b>Key Words:</b> cancer:head & neck,radiotherapy,cisplatin,5-Fluorouracil					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		11/17/95
			\$9130.00		

**Study Objective:** To evaluate the feasibility of administering three courses of chemotherapy to resected patients who have received cisplatin and radiation therapy post-operatively and to evaluate the qualitative and quantitative toxicities.

**Technical Approach:** Patients who have had resected squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx are eligible for the study. Chemotherapy used prior to surgery or radiotherapy in untreated head and neck cancer patients has produced particularly high rates of response. However, previous studies have shown that 20-25% of these patients will refuse further surgery or radiotherapy because of an initial good overall response with chemotherapy alone. To avoid this problem, the chemotherapy in this study will be given after surgery, along with radiation and as maintenance afterwards. Cisplatin, 100 mg/m<sup>2</sup>, on days 1, 22, and 43 will be given concomitant with radiation therapy. Three to four weeks post-radiation therapy, maintenance chemotherapy will be started. Maintenance chemotherapy will consist of cisplatin, 100 mg/m<sup>2</sup>, day 1 every 21 days for three courses and 5-FU, 1000 mg/m<sup>2</sup>, days 1-4, every 21 days for three courses.

**Progress:** This study closed to patient entry 1 May 92. One patient was enrolled in FY92 and is still being followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/021		<b>Status:</b> Completed	
<b>Title:</b> SWOG 8990: (ECOG-9228, INT-0103): Combined Modality Treatment for Resectable Metastatic Colorectal Carcinoma to the Liver; Surgical Resection of Hepatic Metastases in Combination with Continuous .....					
<b>Start Date:</b> 12/07/90			<b>Est. Completion Date:</b> Indefinite		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ William A. Phillips					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Paul C. Sowray, MC			LTC Luke M. Stapleton, MC		
MAJ Everardo E. Cobos Jr., MC			MAJ Patrick L. Gomez, MC		
LTC Robert L. Sheffler, MC			LTC Robert B. Ellis, MC		
CPT Jennifer L. Cadiz, MC			COL Joseph F. Homann, MC		
<b>Key Words:</b> cancer:colorectal, resection, chemotherapy, liver					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		11/17/95	

**Study Objective:** To study the effects of long-term continuous infusion of Floxuridine (FUDR) intra-arterially and 5-FU systemically as therapy for liver metastases from colorectal primaries and to study the incidence of recurrence and time to recurrence in patients with 1-3 hepatic metastases treated with resection and continuous infusion of 5-FU into the systemic venous system and FUDR into the hepatic artery.

**Technical Approach:** This study attempts to combine surgical resection with long term hepatic artery infusion of chemotherapy and continuous infusion 5-FU. Patients with histologic confirmation of colorectal primary carcinoma and evidence of 1-3 liver metastases wither on CAT scan, liver scan or previous laparotomy, with no metastatic disease other than to the liver will be randomized to either surgery plus observation or sugary plus FUDR and 5-FU. FUDR will be given 0.1 mg/kg/day continuously for 14 days via Infusaid pump or arterial subcutaneous device. This cycle will be repeated every 28 days for 4 cycles. 5-FU will be given 200 mg/m<sup>2</sup>/day IV continuously for 14 days via permanent IV access device beginning of day 15 of each 28 day cycle and repeated for 4 cycles. When FUDR therapy ends, the IV dosage of 5-FU will be escalated to 300 mg/m<sup>2</sup>/day IV continuously for 14 days and repeated every 28 days for eight more cycles.

**Progress:** No patients have entered this study at MAMC. It was closed to patient entry, 31 Jan 97.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/131		<b>Status:</b> Completed	
<b>Title:</b> SWOG 8994: Evaluation of Quality of Life in Patients with Stage C Adenocarcinoma of the Prostate Enrolled on SWOG 8794					
<b>Start Date:</b> 08/05/94			<b>Est. Completion Date:</b> Jun 01		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b> None					
<b>Key Words:</b> Cancer:prostate, surgery, radiation therapy					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 11/17/95

**Study Objective:** To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning

**Technical Approach:** This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles will be compared for the two treatment groups at different points in time: baseline, where no differences are expected six weeks, where the two treatment groups are expected to show maximum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key continuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurrence of specified complications, standard methods of categorical data analysis will be employed.

**Progress:** One patient was enrolled in FY95. This is a companion protocol evaluating quality of life on patients enrolled in SWOG 8794. This protocol has been closed to patient entry and this patient will be followed on SWOG 8794.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 90/056	<b>Status:</b> On-going
<b>Title:</b> SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide		
<b>Start Date:</b> 03/16/90	<b>Est. Completion Date:</b> Mar 93	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC		MAJ Everardo E. Cobos Jr., MC
MAJ Patrick L. Gomez, MC		CPT Denis Bouvier, MC
LTC Kenneth A. Bertram, MC		LTC Robert L. Sheffler, MC
LTC John A. Vaccaro, MC		
<b>Key Words:</b> cancer:testicular,chemotherapy,cisplatin,bleomycin,ifosfamide		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$12862.00	11/17/95

**Study Objective:** To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

**Technical Approach:** Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

**Progress:** Prior to closure to patient entry (9 Apr 92) two patients had been enrolled at MAMC. One patient is still being followed (one died Jan 93).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/056		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9003: Fludarabine for Waldenstrom's Macroglobulinemia (WM): A Phase II Study for Untreated and Previously Treated Patients					
<b>Start Date:</b> 03/05/93			<b>Est. Completion Date:</b> Mar 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Howard Davidson, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Kenneth A. Bertram, MC			MAJ Patrick L. Gomez, MC		
MAJ Timothy P. Rearden, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
<b>Key Words:</b> Waldenstrom's Macroglobulinemia					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$3352.00
					11/17/95

**Study Objective:** 1) To estimate response rates and survival in patients with Waldenstrom's Macroglobulinemia (WM) receiving fludarabine, with stratification according to whether they have prior therapy. 2) To define prognostic factors that may relate to response, time to progression and overall survival, separately for newly diagnosed and previously treated patients. 3) To estimate the associated hematologic and non-hematologic toxicities.

**Technical Approach:** Persons with a diagnosis of WM and meeting enrollment criteria can be registered for this study. After the initial workup, to include bone marrow aspiration, those patients without symptoms and with no progression of the disease will be entered in the Observation phase. If they are symptomatic or have progression of the disease or if onset of symptoms and/or progression occurs during the Observation phase immediate Re-registration to the Treatment phase will occur. Fludarabine 30 mg/m<sup>2</sup> IV will be administered on days 1 - 5. This schedule will be repeated every 28 days for 4 cycles until the patient's condition is stable without remission, progression occurs, or the disease is stable. If the disease becomes stable without remission or progresses, treatment will be stopped. If there is complete remission, partial remission or improvement the patient will receive an additional 4 cycles of therapy or 2 cycles beyond maximum response, whichever occurs earlier.

**Progress:** Two patients were enrolled in FY 93 and are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/094		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9007: Cytogenetic Studies in Leukemia Patients, Ancillary					
<b>Start Date:</b> 09/06/91			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>					
MAJ Paul C. Sowray, MC			LTC Howard Davidson, MC		
MAJ Patrick L. Gomez, MC			LTC Luke M. Stapleton, MC		
LTC Robert B. Ellis, MC			LTC Robert L. Sheffler, MC		
CPT Jennifer L. Cadiz, MC			MAJ Richard C. Tenglin, MC		
			MAJ James S. D. Hu, MC		
<b>Key Words:</b> cancer:leukemia,cytogenetic studies					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		11/17/95	

**Study Objective:** To compare these primary aspects of quality of life, according to treatment assignment: 1) Treatment specific symptoms 2) Physical Functioning 3) Emotional functioning To compare three secondary quality of life variables, according to treatment assignment: 1) General symptoms 2) Global perception of quality of life 3) Social functioning

**Technical Approach:** This is a companion to SWOG 8794. Patients will be assigned to the same treatment groups as in the companion protocol (prostatectomy followed by adjuvant radiotherapy versus prostatectomy alone) and must be able to complete a quality of life questionnaire prior to registration and randomization on SWOG-8794. Standardized instructions will be read to the patients by the nurse/data manager at each site. Additional questionnaires will be completed at week 6, 6 months, 12 months, and then yearly for the next 4 years. Quality of life profiles will be compared for the two treatment groups at different points in time: baseline, where no differences are expected six weeks, where the two treatment groups are expected to show maximum differences on some measures; six months, one year and annually for a total for five years, where the treatment means for quality of life measures are expected to come together and level off. For key continuous variables, repeated measures analyses of variance should help to make comparisons at fixed points in time and across time. For the discrete variables such as occurrence or non-occurrence of specified complications, standard methods of categorical data analysis will be employed.

**Progress:** Five patients have been enrolled in previous years. One patient continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 92/051		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9008: Trial of Adjuvant Chemoradiation After Gastric Resection for Adenocarcinoma, Phase II					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b> Mar 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Luke M. Stapleton, MC					
<b>Associate Investigators:</b>					
MAJ Rahul N. Dewan, MC		LTC Howard Davidson, MC			
MAJ Patrick L. Gomez, MC		LTC Kenneth A. Bertram, MC			
LTC Robert L. Sheffler, MC		LTC Robert B. Ellis, MC			
MAJ Richard C. Tenglin, MC		CPT Jennifer L. Cadiz, MC			
		MAJ James S. D. Hu, MC			
<b>Key Words:</b> cancer, gastric, adenocarcinoma, chemoradiation					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		11/17/95	

**Study Objective:** To evaluate the possible benefit of adjuvant chemoradiation therapy in patients with resected gastric cancer to include: comparison of overall and disease free survival between patients being treated with surgical resection only and those being treated with surgery plus adjuvant therapy; comparison of incidence and patterns of disease failure between surgery and surgery plus adjuvant therapy treated patients; and assessment of patient tolerance of upper abdominal chemoradiation after gastric resection.

**Technical Approach:** Patients will be randomized to either observation or adjuvant therapy. Adjuvant therapy will consist of one course of 5-FU and Leucovorin given IV. Four weeks later the patient will receive a second course of 5-FU with Leucovorin with concomitant radiation therapy. While receiving radiation therapy, the patient will receive a third course of 5-FU and Leucovorin, which will occur during the fifth week of radiation therapy. After completing radiation therapy, the patient will receive two additional courses of chemotherapy to begin approximately 35 days after completion of radiotherapy.

**Progress:** One patient was enrolled (FY 94) and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 91/033		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9013 (RTOG 89-11, INT-0113): A Prospective Randomized Comparison of Combined Modality Therapy for Squamous Carcinoma of the Esophagus: Chemotherapy Plus Surgery Versus Surgery Alone for ....					
<b>Start Date:</b> 02/01/91			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>					
MAJ William A. Phillips			LTC Howard Davidson, MC		
MAJ Patrick L. Gomez, MC			LTC Luke M. Stapleton, MC		
LTC Robert B. Ellis, MC			LTC Robert L. Sheffler, MC		
COL Joseph F. Homann, MC			CPT Jennifer L. Cadiz, MC		
MAJ Everardo E. Cobos Jr., MC			COL Daniel G. Cavanaugh, MC		
<b>Key Words:</b> cancer:esophagus,chemotheray,surgery,modality therapy					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b>	
				<b>02/21/97</b>	

**Study Objective:** To compare, using a prospective controlled randomized study design, the outcomes of therapy of surgery alone versus pre and postoperative chemotherapy and surgery for patients with local regional esophageal cancer (outcome is defined as survival and relapse pattern); to assess the toxicities of a multimodality approach to esophageal carcinoma involving systemic chemotherapy and surgery (the toxicities of surgical resection as initial therapy or following chemotherapy will be assessed as operative morbidity and mortality); to compare the local and distant control rates with the two approaches and to define the pattern of failure; and to compare the impact on overall and disease free survival of multimodality therapy with surgery alone.

**Technical Approach:** Esophageal cancer is seen in over 10,000 patients a year in the United States and only about 7% of these patients are cured as demonstrated by a five year survival. This study is designed to see whether or not giving chemotherapy will improve that survival. To be eligible patients must have histologic proof of squamous cell carcinoma of the esophagus, disease limited to the total regional area (clinical stage T1-T3, NX,MO), no prior surgery, radiation therapy, or chemotherapy, and adequate bone marrow, liver function, renal function, and pulmonary reserve. Patients must be physiologically fit for proposed chemotherapy and surgery and be greater than 18 years of age. Patients will be randomized to surgery alone, or to receive three cycles of preoperative cisplatinium and 5-FU and then to undergo definitive surgery followed by two more cycles of cisplatinium and 5-FU, starting two to six weeks after surgery.

**Progress:** This study was closed to patient entry 31 Dec 95. Three patients have entered this study in previous years. Two are being followed and one died of the disease.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/143	<b>Status:</b> On-going
<b>Title:</b> SWOG 9019: A Phase III, Randomized, Prospective Comparison Between Chemotherapy Plus Radiotherapy, and the Same Chemotherapy Plus Radiotherapy Together With Surgery for .... Non-Small Cell Lung Cancer		
<b>Start Date:</b> 06/09/93	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Timothy P. Rearden, MC	LTC Kenneth A. Bertram, MC	
LTC Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
LTC Robert D. Vallion, MC	MAJ James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> cancer:non-small cell lung		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** (1) To assess whether concurrent chemotherapy and radiotherapy, followed by surgical resection, results in a significant improvement in progression-free, overall, and long-term survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2 Positive) and selected IIIB non-small cell lung cancer. (2) To evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastasis.

**Technical Approach:** Patients with regionally advanced non-small cell lung carcinoma will be randomized to one of two arms. Arm I: patients will receive induction radiation therapy to a "tight" field to 4500 cGy. They will receive concurrent cisplatin on days 1 and 8 and on days 29 & 36 with VP-16 days 1-5, repeated on days 29-33 (2 cycles). After completion of induction, patients will be re-evaluated for extent of disease. If there is no progression of the disease, patients will go to exploratory thoracotomy for complete removal of the primary lesion and sampling of nodes.

If the tumor is unresectable or the margins are positive or the mediastinal nodes are positive, an additional 2 cycles of chemotherapy with a radiation boost will be given. Patients who complete the induction phase but have persistent supraclavicular node metastases will also receive 2 more cycles of concurrent chemo-radiotherapy will not go to surgery.

Arm II patients receive "standard" lung field radiation therapy to 4500 cGy and concurrent cisplatin and VP-16 for 2 cycles.

One week prior to completing radiation therapy, patients will be re-evaluated for response. Those patients with no evidence of distant metastases or local progression will continue radiation therapy with no break for an additional 1600 cGy with a boost. They will also receive 2 more cycles of chemotherapy concurrent with radiation.

Any patient who shows local or distant progression after induction chemo-radiation will be taken off protocol.

**Progress:** This study was closed to patient entry 1 Dec 95. Two patients have been enrolled in this study in previous years (1 in FY95). One patient continues to be followed and the other died of the disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 92/052	<b>Status:</b> On-going
<b>Title:</b> SWOG 9031: A Double Blind Placebo Controlled Tiral of Daunomycin and Cytosine Arabinoside With or Without rhG-CSF in Elderly Patients With Acute Myeloid Luekemia, Phase III		
<b>Start Date:</b> 04/03/92		<b>Est. Completion Date:</b> Jun 94
<b>Department:</b> SWOG		<b>Facility:</b> MAMC
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC		
<b>Associate Investigators:</b>		LTC Howard Davidson, MC
MAJ Paul C. Sowray, MC		LTC Luke M. Stapleton, MC
MAJ Patrick L. Gomez, MC		LTC Robert B. Ellis, MC
LTC Robert L. Sheffler, MC		CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC		MAJ James S. D. Hu, MC
<b>Key Words:</b> cancer, leukemia, myeloid		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To compare the complete response rates and duration of survival in patients 56 or older with acute myeloid leukemia (AML) when treated with standard doses of cytosine arabinoside (Ara-C) and daunorubicin (DNR), with or without recombinant human granulocyte-colony stimulating factor (rhG-CSF); to assess the frequency and severity of toxicities of the two treatment regimens; to compare the duration of neutropenia and thrombocytopenia, the total number of febrile days, the number of days of antibiotic therapy, the number and type of infection episodes, and the number of hospital days in patients treated with or without rhG-CSF; and to correlate biological parameters including cell surface immunophenotype, ploidy, and cytogenetics with clinical response.

**Technical Approach:** Patients aged 56 and older with AML will be randomized to receive treatment with either Ara-C/DNR plus rhG-CSF or Ara-C/DNR plus placebo (Ara-C days 1-7, C/DNR days 1-3, and blinded drug begins on day 10) Patients who had regrowth of leukemia during this course of treatment will receive a second identical course of treatment except the blinded drug will not be started until the marrow shows <5% blasts. The blinded drug will not be given in the second induction course if the patient has regrowth of leukemia following the first induction course. Following completion of induction therapy, patients who achieve complete remission will be registered to receive two cycles of post-remission therapy, utilizing the same regimen to which they were originally randomized.

**Progress:** This study closed to patient accrual 1 Jan 95. Two patients have been enrolled in this study in previous years. One is deceased and one is being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 92/095		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9032: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in Blast Phase Chronic Myelogenous Leukemia					
<b>Start Date:</b> 08/07/92			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Kenneth A. Bertram, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			MAJ Patrick L. Gomez, MC		
LTC Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			MAJ James S. D. Hu, MC		
<b>Key Words:</b> cancer, myelogenous, leukemia					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>		11/17/95	
\$0		\$0.00			

**Study Objective:** To compare the duration of survival in patients with chronic myelogenous leukemia (CML) in blast phase, when treated with either chemotherapy (Ara-C/Daunomycin) alone or chemotherapy plus the resistance modifier, cyclosporine-A (CyA); to estimate the frequency of P-glycoprotein expression and its association with blast lineage and prognosis; and to compare the frequency and severity of toxicity of the two treatment regimens.

**Technical Approach:** Patients will be randomized to receive treatment with either Ara-C/Daunomycin alone or Ara-C/Daunomycin + CyA. If the day 14 bone marrow shows less than or equal to a 50% reduction in the absolute blast count per 500 cell differential compared with the pretreatment bone marrow, the patient will be considered a treatment failure and removed from the study. If there is more than a 50% reduction in the blast count as stated above, but the patient has not achieved a complete remission or restored chronic phase status, a second course of the original induction regimen will begin on or after day 21. Patients who do not achieve complete remission or restoration of chronic phase after two inductions will be removed from the protocol. Patients who achieve complete remission or restored chronic phase will receive one course of consolidation therapy (same regimen as for induction therapy).

**Progress:** No patients have been entered at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/062		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9035: Randomized Trial of Adjuvant Immunotherapy with an Allogeneic Melanoma Vaccine for Patients with Intermediate Thickness, Node Negative Malignant Melanoma, Phase III					
<b>Start Date:</b> 01/20/95			<b>Est. Completion Date:</b> Jan 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Richard F. Williams, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			LTC Kenneth A. Bertram, MC		
MAJ James S. D. Hu, MC			LTC Robert B. Ellis, MC		
CPT Diana S. Willadsen, MC			LTC Robert D. Vallion, MC		
			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:melanoma, immunotherapy, vaccine					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0		\$0.00	02/21/97		

**Study Objective:** 1) To compare disease-free survival and overall survival between patients with T3NOM0 malignant melanoma who receive adjuvant immunotherapy with an allogeneic melanoma vaccine versus no adjuvant treatment. 2) To evaluate the toxicity of adjuvant immunotherapy with an allogeneic melanoma vaccine in patients with T3NOI10 malignant melanoma. 3) To explore the interaction between the patients' defined HLA types (i.e., whether they are compatible with the HLA phenotypes of the vaccine) and the vaccine treatment effectiveness in terms of disease-free survival and overall survival.

**Technical Approach:** The study is a randomized study of Interferon Alfa-2b as adjuvant immunotherapy in patients with T3NOM0 malignant melanoma following complete resection. After complete staging, including assessment of any abnormal lymph nodes by biopsy, patients will be randomized either to treatment with four cycles of intramuscular vaccine therapy or observation only and will be followed until death for recurrence

**Progress:** One patient was enrolled in FY95 and is still being followed. The protocol was closed to patient entry, 15 Nov 96.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 91/069	<b>Status:</b> On-going
<b>Title:</b> SWOG 9040 (CALGB-9081, INT-0014): Intergroup Sectal Adjuvant Protocol, A Phase III Study		
<b>Start Date:</b> 06/14/91	<b>Est. Completion Date:</b>	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b>		
MAJ Paul C. Sowray, MC	MAJ Everardo E. Cobos Jr., MC	
MAJ Rahul N. Dewan, MC	MAJ Patrick L. Gomez, MC	
LTC Robert L. Sheffler, MC	LTC Steven S. Wilson, MC	
CPT Jennifer L. Cadiz, MC	LTC Robert B. Ellis, MC	
<b>Key Words:</b> cancer:rectum,5-Fluorouracil,leucovorin,levamisole		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To determine the relative efficacy of: 5-FU; 5-FU plus leucovorin; 5-FU plus levamisole; and 5-FU plus leucovorin and levamisole when combined with pelvic radiation therapy in the treatment of Stages B-2 and C (TNM Stage II and III) rectal cancer. End points used will include local recurrence rates, probability of distant metastases, disease free survival rates, and overall survival.

**Technical Approach:** This will be a 4-armed study with the same radiation therapy program in all arms, but with varying drug regimens as listed in the objective. 5-FU with radiation therapy will comprise the control arm of the study. Patients will be randomized to treatment arms and they will be stratified by type of operation (abdominal perineal or anterior resection); nodal involvement (none, 1-3, or >3); and invasion through bowel wall or into adjacent organs (none, through muscularis propria, or adherence to or invasion of adjacent organs or structures). Each drug regimen will be given alone on days 1-5 and 29-33, followed by radiation therapy (five weeks) with concomitant chemotherapy on days 57-60 and 85-88. The chemotherapy regimen will then be repeated beginning 28 days after the completion of radiation therapy on days 1-5 and 29-33. If evidence of recurrence is obtained, protocol treatment will be discontinued and the patient followed until death. In the absence of recurrent disease, follow-up observations will be continued for a minimum of 5 years after surgery.

**Progress:** This study was closed to patient entry on 22 Nov 92. Three patients were enrolled in previous years and continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/104		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9041: Chemoprevention of Recurrent Adenomas and Second Primary Colorectal Carcinoma. A Phase III Pilot Study.					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:colorectal, chemoprevention, calcium carbonate					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
				<b>11/17/95</b>	

**Study Objective:** This is a preliminary effort towards the long-term research goal of determining whether calcium, as a nutritional supplement, can prevent colorectal adenomas and new primary carcinomas in surgically treated colorectal carcinoma (CRC) patients.

**Technical Approach:** Patients with previously resected colon cancer, Stages 0, I, or II or rectal carcinomas, Stages 0, I are eligible to participate in this study. During the 3 month Run In period, patients will be placed on placebo 3 tablet a day. After successful completion of the Run In (patients must have taken > 80% of tablets) patients will be randomized to regimen A (3 - 600 mg tablets of calcium carbonate daily for 5 years) or regimen b (3 placebo tablets daily for 5 years). The pills will be provided to the patients every three months for the first two years and every six months for the next three years. Patients will be monitored for compliance, hypercalcemia, renal toxicity and gastrointestinal or hepatic toxicity. Endpoint is the efficacy of supplemental oral calcium in reducing recurrence of adenomas or second primary carcinomas.

**Progress:** Seven patients were enrolled in this study in FY 97 for a total of 16 patients who are being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/096		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-FU....					
<b>Start Date:</b> 05/16/97			<b>Est. Completion Date:</b> Apr 00		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
Rakesh Gaur, M.D.					
<b>Key Words:</b> Cancer:head and neck, radiotherapy, cisplatin, 5-FU					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>/ /</b>

**Study Objective:** 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.

**Technical Approach:** Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25% range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatin alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatin and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.

**Progress :** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/032	<b>Status:</b> On-going
<b>Title:</b> SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation....Breast Cancer at High Risk of Recurrence		
<b>Start Date:</b> 12/04/92	<b>Est. Completion Date:</b> Nov 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
LTC Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
LTC Robert D. Vallion, MC	MAJ James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> cancer:breast, chemotherapy, bone marrow transplantation		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and flurouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of ≥ 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should

begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while therapy is ongoing.

Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death).

At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about  $\pm 0.09$ .

The BCG will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used. Then using the variance information given above, the variance of the difference of means at either time should have a variance of about 0.0099, and the covariance between the two times should be about 0.0079. If there is a constant difference in the scores, then the distribution of the test statistic would be approximately noncentral chi-square with 2 degrees of freedom and centrality parameters  $113 \cdot d \cdot d$ . For a 5% level test, this gives a power of 82% for detecting a difference of  $d = 0.3$ .

Progress: One patient has been entered this study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol No.:</b> 94/095		<b>Status:</b> Completed	
<b>Title:</b> SWOG 9109: Neoadjuvant Zoladex and Flutamide in Bulky and Non-Bulky Clinical Stage C Carcinoma of the Prostate, Phase II					
<b>Start Date:</b> 04/01/94			<b>Est. Completion Date:</b> Indefinite		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC					
<b>Associate Investigators:</b>					
COL John C. Norbeck, MC			COL John N. Wettlaufer, MC		
CPT Timothy O. Taylor, MC			LTC Kurt L. Hansberry, MC		
CPT Bradley F. Schwartz, MC			CPT Michael D. Bagg, MC		
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			LTC Kenneth A. Bertram, MC		
			MAJ Timothy P. Rearden, MC		
<b>Key Words:</b> Cancer:prostate, Zoladex, Flutamide					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		11/17/95	

**Study Objective:** 1) To evaluate the resectability rate following 16 weeks of total androgen blockade therapy. 2) To evaluate the likelihood of clinical response to 16 weeks of total androgen blockade therapy. 3) To assess the feasibility of obtaining flow cytometry specimens for the purpose of evaluating the likelihood of an association between ploidy and clinical response or resectability. 4) To evaluate the qualitative and quantitative toxicities from total androgen blockade therapy and the immediate and long-term morbidity associated with radical prostatectomy and pelvic lymph node dissection following neoadjuvant total androgen blockade therapy. 5) To evaluate time to progression.

**Technical Approach:** Patients with Stage C, D0, and D1 prostate cancer will begin neoadjuvant total androgen blockade within 24 hours of registration. This treatment will consist of Zoladex 3.6 mg S.Q. every 4 weeks X 16 weeks and Flutamide 250 mg P.O. daily X 16 weeks. Patients will be evaluated by digital rectal exam at weeks 5, 9, 13 and 17, and trans-rectal ultrasound at weeks 9 and 17. After 16 weeks of androgen blockade, patients will be re-evaluated to undergo radical prostatectomy with pelvic lymph node dissection. Patients deemed operable will have surgery performed by week 17 or, if the treatment was interrupted, within one week of completing total androgen blockade. Following surgery, all patients, including those that were unresectable or partially resectable, will be followed for subjective/objective evidence of developing toxicities and progression of disease. Following surgery or attempted surgery, no additional therapy is to be given in the absence of progression, at which time patients will go off protocol treatment. Subsequent therapy off protocol treatment is at the discretion of the investigator.

**Progress:** No patients entered in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 92/053		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9119: Primary Chemotherapy of Poor Prognosis Soft Tissue Sarcomas, Phase II					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b> Mar 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			LTC Robert B. Ellis, MC		
LTC Robert L. Sheffler, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			MAJ James S. D. Hu, MC		
<b>Key Words:</b> cancer, soft tissue sarcoma, chemotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					11/17/95

**Study Objective:** To evaluate, in patients with high grade soft tissue sarcoma of the extremity, the trunk, or the head and neck, the efficacy of primary chemotherapy, wide surgical resection, adjuvant chemotherapy, and radiotherapy on local control, metastasis free survival, and overall survival; To evaluate the utility of tumor response to primary chemotherapy as an indicator of local and systemic disease control in high grade soft tissue sarcoma; and to evaluate the toxicity of primary chemotherapy, surgery, adjuvant chemotherapy, and radiation therapy in this patient population. Secondary objectives include those listed for SWOG 9136, a companion protocol studying biologic parameters.

**Technical Approach:** Patients with a high grade soft tissue sarcoma of the extremity, trunk, or head and neck area are eligible. Patients will receive chemotherapy using the drugs adriamycin, DTIC, and ifosfamide, given concurrently for three cycles at 21 day intervals. Patients will then undergo wide surgical excision of the primary tumor. Following recovery from surgery, patients with partial or complete response or stable disease will receive another three courses of therapy, followed four weeks after completion of chemotherapy by radiation therapy to the whole area (days 1-5 for 6-8 weeks).

**Progress:** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 92/017		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9125: A Phase II Trial of CVAD/Verapamil/Quinine for Treatment of Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 12/06/91			<b>Est. Completion Date:</b> Oct 92		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Patrick L. Gomez, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
MAJ Paul C. Sowray, MC			LTC Luke M. Stapleton, MC		
LTC Kenneth A. Bertram, MC			LTC Robert L. Sheffler, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
CPT Jennifer L. Cadiz, MC			MAJ James S. D. Hu, MC		
<b>Key Words:</b> cancer, non-Hodgkin's lymphoma, CVAD, verapamil, quinine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objective:** (1) To evaluate the effectiveness of the CVAD chemotherapy regimen (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) when administered in combination with chemosensitizers (verapamil and quinine) which are intended to block the emergence of multidrug resistance in previously untreated patients with intermediate and high grade non-Hodgkin's lymphoma. The effectiveness of CVAD plus verapamil and quinine will be based on the estimate of the complete response rate and the time to treatment failure. (2) To assess the toxicities and side effects associated with the CVAD regimen when combined with verapamil and quinine. Secondary objectives are to further investigate the utility of the proliferative rate (determined by Ki-67 monoclonal antibody), the importance of cell-cell recognition molecules, the role of host response, and the value of detectable levels of p\_glycoprotein as prognostic indicators of outcome in conjunction with companion study SWOG 8819; and to further utilize the central serum repository enabling clinicopathologic correlations with the results of studies on the material collected (see companion study SWOG 8947).

**Technical Approach:** Currently, regardless of the regimen used, 30 to 60% of advanced stage non-Hodgkin's lymphoma patients will relapse and the emergence of clinical drug resistance is a significant problem in these patients. In this study, patients will receive oral verapamil and quinine on days 1-6 as chemosensitizers. They have been shown to reverse the multidrug resistance associated with P-glycoprotein. Starting on day 2, patients will receive a continuous infusion of Adriamycin and vincristine for four days, Cytoxan will be given IV on Day 2 and oral decadron will be given days 2-5. Patients with documented progressive disease at any time will be taken off protocol treatment. Patients with stable disease will receive 2 courses (6 weeks) of chemotherapy. Patients responding to treatment will receive a maximum of 8 courses of chemotherapy. Patients will be restaged upon completion of the treatment program to assess response, with a complete laboratory and radiographic evaluation one month after the completion of therapy. All patients will be followed until death.

**Progress:** This study was closed to patient entry 15 Feb 93. Two patients were enrolled in previous years and are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/154		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9126: A Controlled Trial of Cyclosporine as a Chemotherapy-Resistance Modifier in High Risk Acute Myelogenous Leukemia, Phase III					
<b>Start Date:</b> 08/06/93			<b>Est. Completion Date:</b> Sep 94		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			MAJ Patrick L. Gomez, MC		
LTC Kenneth A. Bertram, MC			MAJ Timothy P. Rearden, MC		
MAJ Richard C. Tenglin, MC			MAJ James S. D. Hu, MC		
CPT Diana S. Willadsen, MC			LTC Robert D. Vallion, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> cancer:leukemia, cyclosporine, Ara-C, daunorubicin					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0	<b>OMA Cost:</b>	\$0.00	11/17/95	

**Study Objective:** 1. To compare the complete remission rate and duration of survival in patients with high-risk AML when treated with either chemotherapy (Ara-C /Daunomycin) alone or chemotherapy plus the resistance modifier cyclosporine-A (CyA). 2. To estimate the frequency of p-glycoprotein expression and the correlation with prognosis in patients with relapsed AML, primarily refractory AML, and secondary AML.

**Technical Approach:** Patients will be randomized to receive either high-dose Ara-C 3 g/m<sup>2</sup>/d on days 1-5 and daunorubicin 45 mg/m<sup>2</sup>/d on days 6-8, a standard induction regimen for poor-prognosis AML or the same therapy plus cyclosporine A. The cyclosporine A will be given as a loading dose of 6.0 mg/kg IV over 2 hours on day 6 starting 8 hours before the daunorubicin, then 4.0 mg/kg over the next 6 hrs, then 16 mg/kg continuous 24 hr infusion beginning concurrently with the daunorubicin on days 6-8. Bone marrow aspirate and biopsy should be performed on day 14 of induction. Subsequent marrow evaluations should be performed every 7 - 14 days to assess response and recovery period to the next course of chemotherapy.

Patients achieving remission will go on to consolidation. Therapy will consist of the same drugs and dosages except ARA-C will be given on days 1-3 and daunomycin on days 4-6. Cyclosporine A will be given on days 4 - 6 as outlined above. No additional protocol directed treatment will be conducted after consolidation.

**Progress:** One patient was enrolled in this study at MAMC in FY93 and one patient in FY 94. Both are now deceased.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 94/097	<b>Status:</b> On-going
<b>Title:</b> SWOG 9133: Randomized Trial of Subtotal Nodal Irradiation versus Doxorubicin Plus Vinblastine and Subtotal Nodal Irradiation for Stage I-IIA Hodgkin's Disease, Phase III		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> Sep 01	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
LTC Robert B. Ellis, MC	MAJ Timothy P. Rearden, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
LTC Robert D. Vallion, MC	MAJ James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> Cancer:Hodgkin's, irradiation, vinblastine, doxorubicin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** The main objective of this study is to compare progression-free and overall survivals of clinically stage (non-laparotomized) patients with early stage (IA,IIA), good-prognosis Hodgkin's Disease treated with either standard subtotal nodal irradiation or with short-course chemotherapy plus standard irradiation. In addition, the study will attempt to identify subgroups of patients who may do better with one approach or the other, and to follow patients for long-term toxicities associated with either regimen.

**Technical Approach:** Patients will be clinically staged by standard methods and then, if they appear to have localized, good-prognosis disease, they will be randomized to receive either standard radiotherapy to mantle and para-aortic fields (subtotal nodal irradiation) or three cycles (6 doses) of chemotherapy followed by the same radiotherapy. Management of both patient groups will be identical apart from the chemotherapy.

**Progress:** Two patients were enrolled in this study, both in FY 94 and continue to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 92/056		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9136: Biologic Parameters in Soft Tissue Sarcomas: A Companion Study to Select Southwest Oncology Group Clinical Trials with Soft Tissue Sarcoma Patients					
<b>Start Date:</b> 04/03/92			<b>Est. Completion Date:</b> Mar 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC					
<b>Associate Investigators:</b>			LTC Howard Davidson, MC		
LTC Luke M. Stapleton, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			LTC Robert B. Ellis, MC		
LTC Robert L. Sheffler, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			MAJ James S. D. Hu, MC		
MAJ George F. Hodeges, MC					
<b>Key Words:</b> cancer, soft tissue sarcomas,biologic parameters					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
				11/17/95	

**Study Objective:** (1) To develop a cooperative group mechanism to study biologic parameters of soft-tissue sarcomas in patients entered onto companion SWOG protocols (see SWOG 9119).;(2) To determine cellular DNA content parameters (DNA CCP) (DNA Ploidy, S-Phase Fraction) of soft tissue sarcomas and to evaluate the effect of these parameters on disease free survival and overall survival. To study the changes in DNA CCP as a result of chemotherapy, and the relationship of these changes to prognosis in patients with soft tissue sarcoma.;(3) To characterize cytogenetic aberrations of soft-tissue sarcomas in the study population. To evaluate the relationship of defined cytogenetic abnormalities to prognosis.;(4) To estimate the level of expression of the multi-drug resistant (MDR) phenotype in untreated soft-tissue sarcoma, and the effect of chemotherapy treatment on the expression of MDR. To evaluate the impact of MDR expression on response to chemotherapy, disease free survival, and overall survival. ;(5) To provide a repository of frozen tissue for future molecular studies in this group of patients.

**Technical Approach:** As a companion protocol to SWOG 9119 (adjuvant soft-tissue sarcoma trial), DNA CCP, tumor karyotypes, and estimation of the expression of the MDR phenotype of sarcomas entered onto trial will be done.

**Progress:** No patients have entered this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 92/054	<b>Status:</b> Completed
<b>Title:</b> SWOG 9139: Adjuvant Therapy of Primary Osteogenic Sarcomas, Phase II		
<b>Start Date:</b> 04/03/92	<b>Est. Completion Date:</b> Indefinite	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Paul C. Sowray, MC		
<b>Associate Investigators:</b>		
LTC Luke M. Stapleton, MC	LTC Howard Davidson, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
LTC Robert L. Sheffler, MC	LTC Robert B. Ellis, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
	MAJ James S. D. Hu, MC	
<b>Key Words:</b> cancer, osteogenic sarcoma		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	11/17/95

**Study Objective:** To estimate the time to treatment failure and survival rate of the three drug combination, Adriamycin, cisplatin, and ifosfamide, as an adjunctive treatment of osteosarcoma of the extremity; to evaluate histopathologic tumor necrosis following preoperative therapy with this regimen; to assess the feasibility of determining histopathologic tumor necrosis in a cooperative group setting; to assess the influence of clinical prognostic variables on disease outcome; and to assess the toxicity of this regimen.

**Technical Approach:** Primary osteosarcoma is an uncommon malignancy but it is associated with only a 20% cure rate, if no more than surgery is used. Chemotherapy increases survival to above 50%, but whether or not this survival could be further increased has to be determined. The current study uses three drugs (Adriamycin, cisplatin, and ifosfamide) in an alternating fashion with the intent of optimizing treatment prior to surgery. Once four cycles of treatment have been completed, surgery will be undertaken. After recovery from surgery, four more cycles of chemotherapy will be given.

**Progress:** One patient was entered on protocol FY 96. This patient was transferred to follow-up at Kessler AFB. The protocol was closed to patient entry, 1 Dec 96.

### Detail Summary Sheet

**Date:** 30 Sep 97      **Protocol no.:** 93/042      **Status:** Completed

**Title:** SWOG 9152 (EST-4890): Prediction of Recurrence and Therapy Response in Patients with Advanced Germ Cell Tumors by DNA Flow Cytometry

**Start Date:** 02/05/93      **Est. Completion Date:** Jan 95

**Department:** SWOG      **Facility:** MAMC

**Principal Investigator:** MAJ Timothy P. Rearden, MC

<b>Associate Investigators:</b>	LTC Luke M. Stapleton, MC
LTC Howard Davidson, MC	LTC Kenneth A. Bertram, MC
MAJ Patrick L. Gomez, MC	MAJ Mark E. Robson, MC
LTC Robert B. Ellis, MC	CPT Jennifer L. Cadiz, MC
MAJ Richard C. Tenglin, MC	MAJ James S. D. Hu, MC
LTC Robert D. Vallion, MC	CPT Diana S. Willadsen, MC

**Key Words:** cancer:germ cell, DNA flow cytometry

<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b>	<b>OMA Cost:</b>	
\$0	\$0.00	02/21/97

**Study Objective:** (1) To determine the proliferative activity and presence of aneuploidy within paraffin-embedded histopathologic specimens from patients with advanced disseminated (poor prognosis) GCT; (2) to correlate proliferative activity and aneuploidy with clinical features including response to therapy, relapse-free survival, and overall survival in patients entered on ECOG protocol EST 3887/SWOG 8997/CALGB 8991; Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin plus Etoposide with either Bleomycin or Isosfamide.

**Technical Approach:** All pathologic materials will be obtained during the routine diagnostic evaluation of patients registered on EST 3887/SWOG 8997 CALGB 8991. Following pathologic analysis of blocks to determine adequacy of tissue, tissue will be prepared for flow cytometry analysis. Three 50 micron sections will be cut, deparaffinized and rehydrated, enzymatically digested, and stained with the DNA intercalating agent propidium iodide. The florescence of propidium iodide-stained nuclei will be measured on a Coulter 753 tunable dye laser following filtration through a 53 micron nylon mesh. Evaluation of the DNA index (ploidy status) and proliferative activity (cell cycle compartment analysis and proliferative index) will then proceed.

**Progress:** This study closed to patient entry 1 Feb 95. Two patients were enrolled in FY93. This protocol has been closed to patient entry and the one patient who is still be followed will be followed on the treatment protocol. One patient died of heart disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/042	<b>Status:</b> On-going
<b>Title:</b> SWOG 9201 (RTOG 91-11): Phase III Trial to Preserve the Larynx: Induction Chemotherapy and Radiation Therapy versus Concomitant Chemotherapy and Radiation Therapy Versus Radiation		
<b>Start Date:</b> 12/19/96	<b>Est. Completion Date:</b> Nov 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
MAJ Richard F. Williams, MC	LTC Robert B. Ellis, MC	
Rakesh Gaur, M.D.	MAJ John R. Caton, MC	
MAJ Nyun C. Han, MC	LTC Steven S. Wilson, MC	
CPT Brent L. Kane, MC	MAJ Mark E. Shaves, MC	
<b>Key Words:</b> Cancer:larynx, radiation, cisplatin, 5-FU		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	//

**Study Objective:** The normal treatment of cancer of the throat is surgery with removal of the voice box. The purpose of this study is to try to preserve the larynx by using a non-surgical treatment. Three treatments will be compared: 1) chemotherapy followed by radiation, or 2) chemotherapy given at the same time as radiation, or 3) radiation alone.

**Technical Approach:** Treatment 1: Cisplatin and 5-FU will be given twice 3 weeks apart. Treatment 2: Cisplatin will be given once every 21 days (for three doses on Days 1, 22, and 43) during radiation which is given once a day, 5 days a week for 7 weeks. Radiation can be given on an outpatient basis. Cisplatin is given into the vein over 20-30 minutes. 5-FU is given into the vein by continuous infusion over 120 hours following cisplatin administration in Treatment 1.

**Progress :** No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/097	<b>Status:</b> On-going
<b>Title:</b> SWOG 9205: Central Prostate Cancer Serum Repository Protocol		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> Mar 95	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert L. Sheffler, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Luke M. Stapleton, MC	
MAJ Mark E. Robson, MC	MAJ Patrick L. Gomez, MC	
CPT Jennifer L. Cadiz, MC	LTC Robert B. Ellis, MC	
MAJ James S. D. Hu, MC	MAJ Richard C. Tenglin, MC	
CPT Diana S. Willadsen, MC	LTC Robert D. Vallion, MC	
	MAJ Timothy P. Rearden, MC	
<b>Key Words:</b> Cancer:prostate, serum repository		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	09/19/97

**Study Objective:** 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

**Technical Approach:** This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols.

All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator.

**Progress:** Two patients were enrolled in this serum study in FY 97. Two patients were enrolled in previous years; one expired in FY 96 and the other continues to be followed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/115		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9208: Health Status and Quality of Life in Patients With Early Stage Hodgkin's Disease: A Companion Study to SWOG 9133					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Timothy P. Rearden, MC		
MAJ Mark E. Robson, MC			LTC Robert B. Ellis, MC		
MAJ Richard C. Tenglin, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:Hodgkin's, quality of life					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
				<b>11/17/95</b>	

**Study Objective:** 1) To evaluate prospectively the health status and quality of life (QOL) of early stage Hodgkin's Disease patients receiving either subtotal nodal irradiation or short course chemotherapy plus subtotal nodal irradiation. 2) To describe the short-term, acute effects of two treatments for early stage Hodgkin's Disease patients on patient report of symptoms and on patient QOL. 3) To evaluate the intermediate and long-term effects of two treatments for early stage Hodgkin's Disease patients on patient QOL over five years.

**Technical Approach:** Patients enrolled in the companion protocol, SWOG-9133, will be asked to complete questionnaires before registration into this study, at 6 months; and annually for seven years. These questionnaires seek to identify and quantitate those differences pertaining to quality of life issues that the added chemotherapy may have in early stage Hodgkin's disease patients.

**Progress:** No patients have been enrolled in this study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/107		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9210: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma Comparison of (1) VAD-P to VAD-P/Quinine for Induction; (2) Randomization of Prednisone Dose Intensity for ....					
<b>Start Date:</b> 05/07/93			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Kenneth A. Bertram, MC			MAJ Patrick L. Gomez, MC		
MAJ Timothy P. Rearden, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			CPT Jennifer L. Cadiz, MC		
MAJ Richard C. Tenglin, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC					
<b>Key Words:</b> Cancer:myeloma, VAD-P, VAD-P,Quinine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objective:** 1) To compare the effectiveness of the VAD-P chemotherapy regimen when administered alone or in combination with the chemosensitizer quinine intended to block the emergence of multidrug resistance during remission induction in previously untreated patients with multiple myeloma. 2) To evaluate the chemosensitizing potential of quinine to reverse drug resistance in myeloma patients randomized to VAD-P induction who fail to achieve at least 25% regression with chemotherapy alone. 3) To compare the value of alternate day prednisone 10 mg versus 50 mg for remission maintenance for patients proven to achieve at least 25% regression.

**Technical Approach:** Patients with proven multiple myeloma (all stages) who have not received prior chemotherapy are eligible for participation in this trial. A dynamic allocation scheme will be used to randomize patients to one of the two induction treatment arms. INDUCTION: ARM I patients will receive Vincristine 0.4 mg IV q.d. on days 1-4, Doxorubicin 9 mg/m<sup>2</sup> q.d. IV on days 1-4, Dexamethasone 40 mg q.d. PO on days 1-4, and Prednisone 50 mg Q.O.D. on days 9, 11, 13, 15, 17, and 19. This cycle will be repeated Q 21 days for a minimum of 6 to 8 cycles (6 months) or a maximum of 17 cycles (12 months). Patients who fail to achieve  $\geq 25\%$  tumor regression after 12 months of treatment on Arm I (VAD-P) or relapse or progress on Arm I, will be eligible for crossover to VAD-P/Q. ARM II and Crossover schedule patients will receive VAD-P as outlined above on days 2-5 and will also receive Quinine 400 mg t.i.d. on days 1-6 (VAD-P/Q). Patients with  $\geq 25\%$  tumor regression after 9 to 12 months of induction therapy or patients who achieve  $\geq 50\%$  tumor regression after 6 months of induction therapy will be randomized to either of two maintenance regimens. If, in the judgement of the physician the patient will continue to benefit from induction therapy, they may continue up to 12 months. MAINTENANCE: ARM III patients will receive Prednisone, 10 mg Q.O.D., until relapse and ARM IV patients will receive Prednisone 50 mg Q.O.D. until relapse.

**Progress:** One patient was enrolled in FY 94 and died of his disease 9/30/97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/010		<b>Status:</b> On-going
<b>Title:</b> SWOG 9217: Chemoprevention of Prostate Cancer with Finasteride (Proscar), Phase III, Intergroup				
<b>Start Date:</b> 10/01/93		<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG		<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ J. Brantley Thrasher, MC				
<b>Associate Investigators:</b> None				
<b>Key Words:</b> Cancer:prostate, Finasteride				
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>
\$0		\$0.00		09/20/96

Study Objective: The primary objective of this trial will be to determine if finasteride can reduce the development of prostatic cancer in males 55 years and older.

Technical Approach: Men who have attained 55 years of age have never been diagnosed as having prostatic cancer will be randomized to receive Finasteride 5 mg or Matched Placebo PO daily for 7 years. Patients will be followed with clinic visits at 6 months, 1 year and then annually. Annual laboratory screening will include PSA. Triggers are in place to initiate prostatic biopsies. The final endpoint is biopsy proven presence/absence of carcinoma of the prostate after seven years.

Progress: Approximately 50 patients have been enrolled in this study and continue to receive treatment. The protocol has been closed to patient entry.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 95/023	<b>Status:</b> On-going
<b>Title:</b> SWOG 9219: A Phase II Evaluation of Interleukin-4 (IL-4) in Patients With Non-Hodgkin's Lymphoma or Hodgkin's Disease		
<b>Start Date:</b> 11/18/94	<b>Est. Completion Date:</b> Nov 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	LTC Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	LTC Robert B. Ellis, MC	
MAJ Richard F. Williams, MC	CPT Diana S. Willadsen, MC	
	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:Hodgkin's, Cancer:Non-Hodgkin's, Interleukin-4		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	11/17/95

**Study Objective:** 1) To assess the response rate of refractory low grade non-Hodgkin's lymphoma, refractory intermediate or high grade non-Hodgkin's lymphoma and refractory Hodgkin's disease treated with interleukin-4, and 2) to assess the qualitative and quantitative toxicities of interleukin-4 administered in a Phase II study.

**Technical Approach:** Following pretreatment with acetaminophen (650 mg PO) to prevent chills and fever, patients will receive a subcutaneous injection of interleukin-4 (at an initial dose of 3 ug/kg daily for 28 days). Patients must be observed in a medical facility for at least 2 hours after the first 2 daily injections. If no significant side effects occur the patient or family member will be instructed on how to administer subsequent injections at home. Patients will be reevaluated after 28 days with a possible rest period of one or two weeks between 28 day cycles of this treatment.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/136	<b>Status:</b> On-going
<b>Title:</b> SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer		
<b>Start Date:</b> 07/02/93	<b>Est. Completion Date:</b> Jul 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
LTC Robert B. Ellis, MC	MAJ Mark E. Robson, MC	
MAJ Richard C. Tenglin, MC	CPT Jennifer L. Cadiz, MC	
MAJ Timothy P. Rearden, MC	MAJ James S. D. Hu, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> cancer:non-small cell lung, 13-cis retinoic acid		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** Ten patients have been enrolled in this study (1 in FY 97). Two expired in FY 96, and one has been permanently transferred to Keesler AFB. Seven are still being followed at MAMC

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/108	<b>Status:</b> On-going
<b>Title:</b> SWOG 9237: Evaluation of Topotecan in Refractory and Relapsing Multiple Myeloma		
<b>Start Date:</b> 05/07/93	<b>Est. Completion Date:</b> May 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Patrick L. Gomez, MC	LTC Kenneth A. Bertram, MC	
MAJ Mark E. Robson, MC	MAJ Timothy P. Rearden, MC	
CPT Jennifer L. Cadiz, MC	LTC Robert B. Ellis, MC	
LTC Robert D. Vallion, MC	MAJ Richard C. Tenglin, MC	
	CPT Diana S. Willadsen, MC	
<b>Key Words:</b> Cancer:myeloma; topotecan		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** (1) To evaluate the response rate for refractory myeloma treated with topotecan; (2) To evaluate the qualitative and quantitative toxicities of topotecan administered in a Phase II study; (3) To measure topoisomerase levels in multiple myeloma cells.

**Technical Approach:** Patients with proven multiple myeloma, with protein criteria present, who have received exactly one prior regimen, and have shown, in the opinion of the investigator, to have disease progression are eligible for this study. All patients will receive topotecan 1.25 mg/m<sup>2</sup> q.d. IV over 30 minutes on days 1-5 repeated q 21 days. This schedule will continue as long as patients show complete remission, partial remission or stable disease and toxicity is acceptable. Topotecan dosage can be adjusted on nadir counts of the preceding cycle.

It is assumed that topotecan will be of interest if a true response rate of 20% or more is achieved in the treatment of patients with relapsed or refractory multiple myeloma.

**Progress:** This study closed to patient accrual 1 Feb 95. One patient was entered in this study in FY93 and continues to be followed.

# Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 93/092		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9245: Central Lymphoma Repository Tissue Procurement Protocol for Relapse or Recurrent Disease					
<b>Start Date:</b> 04/02/93			<b>Est. Completion Date:</b> May 95		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Patrick L. Gomez, MC			LTC Kenneth A. Bertram, MC		
LTC Robert B. Ellis, MC			MAJ Timothy P. Rearden, MC		
MAJ Richard C. Tenglin, MC			CPT Jennifer L. Cadiz, MC		
CPT Diana S. Willadsen, MC			MAJ James S. D. Hu, MC		
			LTC Robert D. Vallion, MC		
<b>Key Words:</b> cancer:lymphoma, tissue procurement					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
				<b>Periodic Review:</b>	
				<b>11/17/95</b>	

**Study Objective:** 1. To acquire fresh snap-frozen lymphoma tissue from patients who relapse or have recurrent disease after being treated on Southwest Oncology Group treatment protocols. 2. To establish a standard set of procedures for routine acquisition, banking, and study of lymphoma tissues within the cooperative group. 3. To use the repository tissue to establish clinical correlations via presently activated phenotyping studies and future projected molecular studies assessing specimen DNA and RNA status. 4. To examine the biology of therapy failure in relationship to changes in pretreatment and post-therapy immunophenotypic data.

**Technical Approach:** Fresh frozen tissues will be acquired from relapsed patients for basic science protocols, both current and future, designed to better define the biology of relapsed non-Hodgkins's lymphoma. This is not a treatment protocol, nor will results be used to guide treatment decisions.

Fresh biopsies (from any organ site) will be snap-frozen and submitted with one stained (Hematoxylin and Eosin) histologic section with accompanying pathology report to The Department of Pathology at the University of Arizona in Tucson.

**Progress:** No patients have entered this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/161		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9250 (INT-0136): Phase III Intergroup Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Levamisole for Patients With Colon Cancer					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Robert B. Ellis, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Timothy P. Rearden, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:colon, resection, chemotherapy:perioperative, 5FU, levamisole					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					11/17/95

**Study Objective:** To determine if (1) adjuvant therapy with one week of continuous 5-FU given within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging the disease free interval and increasing survival in patients who are treated with 5-FU/Levamisole only. Endpoints include: treatment failure - as described by recurrence of local/regional or distant metastases - and survival. (2) To establish within ECOG a Central Tissue Repository for paraffin blocks and a frozen tissue bank.

**Technical Approach:** Patients with primary colon cancer will be randomized to either receive 7 days of continuous intravenous 5-fluorouracil (5-FU) within 24 hours completion of colon surgery or not to receive any perioperative chemotherapy.

The only investigational part of this protocol is the administration of chemotherapy during the period right after subjects colon operation. The operation and the use of 5-FU/levamisole are all standard treatment.

**Progress:** No patients have been enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/105		<b>Status:</b> Completed	
<b>Title:</b> SWOG 9252: Prospective Randomized Trial of Postoperative Adjuvant Therapy in Patients with Completely Resected Stage II and Stage IIIa Non-small Cell Lung Cancer, Intergroup					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> Indefinite		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:lung, non-small cell, cisplatin, etoposide					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b> \$0.00		<b>OMA Cost:</b> \$0.00		11/17/95	

**Study Objective:** 1) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in prolonging survival in patients with completely resected Stage II and IIIa non-small cell lung cancer. 2) To determine if combination chemotherapy plus thoracic radiotherapy is superior to thoracic radiotherapy alone in preventing local recurrence in patients with resected Stage II or IIIa non-small cell lung cancer.

**Technical Approach:** Patients who have undergone a surgery for Stage II or IIIa disease are eligible to participate in this trial. Patients will be stratified for nodal status (N1, N2), histology (squamous, other), weight loss in previous 6 months (< 5%, >= 5%), and lymph node dissection (sampling, complete node resection). After stratification they will be randomized to receive radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) alone or radiotherapy treatment (50.4 Gy/28 fractions/6 weeks) concurrent with Cisplatin (DDP) 60 mg/m<sup>2</sup> IV days 1, 29, 57, 85 and Etoposide (VP-16) 120 mg/m<sup>2</sup> IV days 1, 2, 3; 29, 20, 31; 57, 58, 59; 85, 86, 87. Patients will be followed for 5 years. The statistical analysis will be based mainly on the stratified logrank test for comparison of two treatments. The second endpoint of local recurrence rate will be also analyzed as will the time to recurrence.

**Progress:** One patient has been enrolled in this study at MAMC in FY95 and is now deceased. The protocol was closed to patient entry in 1 Dec 96.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 94/073	<b>Status:</b> On-going		
<b>Title:</b> SWOG 9300: A Randomized Phase II Evaluation of All Trans-Retinoic Acid with Interferon-Alfa 2a or All Trans-Retinoic Acid with Hydroxyurea.... Diagnosed Chornic Myelogenous Leukemia in Chronic Phase				
<b>Start Date:</b> 03/04/94	<b>Est. Completion Date:</b> Mar 94			
<b>Department:</b> SWOG	<b>Facility:</b> MAMC			
<b>Principal Investigator:</b> MAJ Mark E. Robson, MC				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <b>Associate Investigators:</b>  LTC Howard Davidson, MC  MAJ Patrick L. Gomez, MC  LTC Robert B. Ellis, MC  MAJ James S. D. Hu, MC  CPT Diana S. Willadsen, MC </td> <td style="width: 50%; vertical-align: top;"> LTC Luke M. Stapleton, MC  LTC Kenneth A. Bertram, MC  MAJ Timothy P. Rearden, MC  MAJ Richard C. Tenglin, MC  LTC Robert D. Vallion, MC  MAJ Richard F. Williams, MC </td> </tr> </table>			<b>Associate Investigators:</b> LTC Howard Davidson, MC MAJ Patrick L. Gomez, MC LTC Robert B. Ellis, MC MAJ James S. D. Hu, MC CPT Diana S. Willadsen, MC	LTC Luke M. Stapleton, MC LTC Kenneth A. Bertram, MC MAJ Timothy P. Rearden, MC MAJ Richard C. Tenglin, MC LTC Robert D. Vallion, MC MAJ Richard F. Williams, MC
<b>Associate Investigators:</b> LTC Howard Davidson, MC MAJ Patrick L. Gomez, MC LTC Robert B. Ellis, MC MAJ James S. D. Hu, MC CPT Diana S. Willadsen, MC	LTC Luke M. Stapleton, MC LTC Kenneth A. Bertram, MC MAJ Timothy P. Rearden, MC MAJ Richard C. Tenglin, MC LTC Robert D. Vallion, MC MAJ Richard F. Williams, MC			
<b>Key Words:</b> Cancer:leukemia, chronic myelogenous, trans-retinoic acid, alpha interferon, hydroxyurea				
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>		
\$0	\$9686.00	11/17/95		

**Study Objective:** 1). To estimate whether treatment of Chronic Myelogeneous Leukemia (CML), with all-trans retinoic acid in combination with either hydroxyurea or interferon alfa-2a is sufficiently effective based on either hematologic or cytogenetic response, to justify its investigation in phase III trials. 2). To assess the toxicities associated with all-trans retinoic acid plus hydroxyurea or itnerferon alfa-2a in chronic phase CML.

**Technical Approach:** Patients qualifying for this study will be stratified by age (< 45 vs ≥ 45), splenomegaly (present vs absent), prior hydroxyurea (yes or no), and ANC at diagnosis (<50,000  $\mu$ l). Patients will then be randomized to one of two treatment arms as follows: Arm I: ATRA and HU or Arm II: ATRA and IFN. This randomization will be dynamically balanced to assure roughly equal numbers of patients within levels of the stratifying factors. All patients in both arms will begin treatment with HU to control or keep the WBC  $\leq$  20,000/ $\mu$ l and platelets  $\leq$  800,000/ $\mu$ l. All therapy will include allopurinol. Patients will receive this HUS treatment for a minimum of 21 days and a maximum of 42 days. Patients with WVA  $\leq$  20,000/ $\mu$ l, platelets  $\leq$  800,00/ $\mu$ l, and no evidence of progressive splenomegaly after 21 - 42 days of HU will then bergin treatment on their assigned regimens. Patients who do not achieve a WBC  $\leq$  20,000/ $\mu$ l, platelets  $\leq$  800,000/ $\mu$ l, and absence of progressive splenonegaly after 42 days will be removed from protocol treatment. Arm I patients will receive ATRA 150/mg/m<sup>2</sup>/d x 7 days followed by 7 days rest and HU 500 mg qd adjusted to maintain WBC and platelets to predefined levels. Arm II patients will receive acetaminophen 650 mg 1/2 hr before administration of IFN initiated a 3 MIU/m<sup>2</sup>/d 5 days/week escalated by 1 MIU/m<sup>2</sup> each week to a maximum of 5 MIU/m<sup>2</sup>/day and ATRA 150 mg/m<sup>2</sup>/d x 7 days followed by 7 days rest. Treatment regimens will continue until the onset of accelerated or blast phase or relapse from CR or PR. Bone marrow aspiration and biopsy to monitor disease status are required at 3 and 6 months and every 6 months thereafter. Serial blood and urine specimens will be obtained for laboratory analysis.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 93/166	<b>Status:</b> On-going
<b>Title:</b> SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer		
<b>Start Date:</b> 09/03/93	<b>Est. Completion Date:</b> Oct 98	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC		
<b>Associate Investigators:</b>		LTC Luke M. Stapleton, MC
LTC Kenneth A. Bertram, MC		MAJ Patrick L. Gomez, MC
MAJ Mark E. Robson, MC		LTC Robert B. Ellis, MC
MAJ Richard C. Tenglin, MC		MAJ James S. D. Hu, MC
LTC Robert D. Vallion, MC		CPT Diana S. Willadsen, MC
MAJ Richard F. Williams, MC		MAJ John R. Caton, MC
<b>Key Words:</b> cancer:colon, irradiation, levamisole, 5-FU		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	11/17/95

**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T<sub>4</sub>BN<sub>0</sub>-2 colon cancer and selected patients with T<sub>3</sub>N<sub>1</sub>-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** This study was closed to patient entry, 17 Dec 96. One patient has been enrolled in this study at MAMC in FY95 and continues to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/111		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9304: Postoperative Evaluation of 5-FU by Bolus Injection vs 5-FU by Prolonged Venous Infusion Prior to and Following Combined Prolonged Venous + Pelvic XRT vs Bolus 5-FU +Leucovorin + ...					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:rectal, 5-FU, Leucovorin, Levamisole, radiotherapy					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		11/17/95	

**Study Objective:** 1) To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged venous infusion given prior to and following combined pelvic x-ray (XRT) therapy + protracted venous infusion (PVI) vs. 5-FU by bolus injection plus LV plus LEV given prior to and following combined pelvic XRT plus bolus 5-FU plus LV in the treatment of modified Aster-Coller Stages B2, B3 and C rectal cancer. This will be evaluated in terms of survival and relapse-free survival.;2) To obtain descriptive information regarding relapse patterns and tolerance.

**Technical Approach:** Patients entering this study will be randomized to one of three treatment arms. Patients in all arms will receive pelvic radiotherapy. Those randomized to Arms A and B will receive concomitant 5-FU by PVI (225 mg/m<sup>2</sup>/d) during radiotherapy. Each patient will be randomly allocated to receive 5-FU +- LV and levamisole for 2 months prior to and for 2 months following combined chemo-radiotherapy. Patients will be randomized to chemotherapy prior to and following chemo-radiotherapy as follows: ;a. Arm A: bolus IV injection of 5-FU alone;b. Arm B: protracted venous infusion of 5-FU alone;c. Arm C: bolus 5-FU + LV + levamisole before and after pelvic radio therapy; bolus 5-FU + LV during pelvid radiotherapy. After completion of all therapy patients will be followed every 4 months X 2 years, then every 6 months X 4 years.

**Progress:** Three patients have been enrolled in this study at MAMC. One patient expired in FY 96, two continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol No.:</b> 94/106	<b>Status:</b> Completed
<b>Title:</b> SWOG 9308: Randomized Trial Comparing Cisplatin With Cisplatin Plus Intravenous Navelbine in the Treatment of Previously Untreated, Stage IV Non-small Cell Lung Cancer Patients		
<b>Start Date:</b> 05/06/94	<b>Est. Completion Date:</b> Indefinite	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Robert B. Ellis, MC		
<b>Associate Investigators:</b>		LTC Luke M. Stapleton, MC
LTC Howard Davidson, MC		LTC Kenneth A. Bertram, MC
MAJ Patrick L. Gomez, MC		MAJ Timothy P. Rearden, MC
MAJ Mark E. Robson, MC		MAJ Richard C. Tenglin, MC
MAJ James S. D. Hu, MC		LTC Robert D. Vallion, MC
CPT Diana S. Willadsen, MC		MAJ Richard F. Williams, MC
<b>Key Words:</b> Cancer:lung, non-small cell, cisplatin, Navelbine		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0.00	<b>OMA Cost:</b> \$0.00	11/17/95

**Study Objective:** 1) Compare the effect of cisplatin alone with that of intravenous Navelbine plus cisplatin on tumor response rate, survival, and time to treatment failure in patients with Stage IV non-small cell lung carcinoma. 2) Compare the toxicity of the two treatment regimens in patients with Stage IV non-small cell lung carcinoma.

**Technical Approach:** At the time of registration, patients will be stratified by LDH (normal vs abnormal) and classified by the following: a. disease status (measurable vs. evaluable), b. prior surgical resection or RT (yes vs. no), c. histology (squamous cell vs. large cell vs. adenocarcinoma vs. unspecified). They will then be randomized to either of two arms. Arm I patients will receive Cisplatin 100 mg/m<sup>2</sup> over 30 - 60 minutes every 28 days X 4. Arm II patients will receive Navelbine 25 mg/m<sup>2</sup> repeated weekly X 16 plus Cisplatin 100 mg/m<sup>2</sup> over 30 - 60 minutes every 28 days X 4. Patients will be evaluated every 3 months for the first year, every 6 months the second year, then yearly thereafter.

**Progress:** This study closed to patient accrual 1 June 95. One patient was enrolled in FY 95 and expired 25 Oct 96.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/170		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast.... 0-3 Positive Nodes					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Robert B. Ellis, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Timothy P. Rearden, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> cancer:breast, chemotherapy, cyclophosphamide, doxorubicin, positive nodes					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		11/17/95

**Study Objective:** 1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide. 2) To obtain tumor tissue for biologic studies.

**Technical Approach:** Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.

**Progress:** The protocol was closed to patient entry, 15 Apr 97. One patient has been enrolled in this study at MAMC and is being followed.

# **Detail Summary Sheet**

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/107		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9321: Standard Dose Versus Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma, Phse III					
<b>Start Date:</b> 05/06/94			<b>Est. Completion Date:</b> May 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Timothy P. Rearden, MC		
MAJ Mark E. Robson, MC			LTC Robert B. Ellis, MC		
MAJ Richard C. Tenglin, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:myeloma, BCNU, Cyclophosphamide, Cyclosporine, Dexamethasone, Doxorubicin, G-CSF, Interferon-alpha 2b, Melphalan, Mesna, Methotrexate, Prednisone, Vincristine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
				<b>11/17/95</b>	

**Study Objective:** 1) To perform a randomized trial, in newly diagnosed patients with symptomatic multiple myeloma (MM), of standard therapy versus myeloablative therapy, in order to examine whether the greater tumor cytoreduction effected by intensive therapy and manifested by higher incidence of complete remission translates into extended overall survival and progression-free survival. 2) To randomize responding patients with  $\geq 75\%$  tumor cytoreduction to interferon-alpha 2b (IFN) versus no maintenance in order to evaluate the role of IFN in MM.

**Technical Approach:** Symptomatic patients of all stages of multiple myeloma with reasonable performance status will be randomized to high dose chemotherapy with autologous bone marrow transplant or standard VBMCP combination chemotherapy after induction VAD therapy. A required peripheral stem cell harvest will be done for those randomized to the ABMT arm for future high dose therapy if failure occurs. This will be an option for those randomized to the standard arm. Those patients that have an HLA compatible sibling donor will be eligible for allogeneic BMT. A second randomization will be done for those with continued greater than 75 percent regression of disease in the ABMT or standard chemotherapy arm while those receiving allo-BMT will be continued on GVHD prophylaxis.

**Progress:** No patients have been enrolled in this study at MAMC.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/114		<b>Status:</b> Completed	
<b>Title:</b> SWOG 9323: Laboratory/Clinical Correlative Studies in Non-Small Cell Lung Cancer: Ancillary Study to SWOG 9252 (INT-0115, E3590, RTOG 91-05, NCCTG 91-24-51)					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Indefinite		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:lung, K-ras, p53, antigen, EHF receptor levels, p105, Factor 8					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>	\$0.00	<b>OMA Cost:</b>	\$0.00	11/17/95	

**Study Objective:** 1) To determine the incidence of K-ras and p53 mutations; assess Group A blood antigen and EHF receptor levels; and assess p105 and Factor 8 levels in patients with completely resected Stage II or IIIa SCLC. 2) Correlate these results with patient histology, TNM stage, time to relapse, and survival.

**Technical Approach:** SWOG 9323 requires that tissue samples of lung cancer resected from each patient enrolled on SWOG 9252 be sent to three central research laboratories. Investigators will study the tissue samples for the tumor markers, K-ras, p-53, and others. Investigators are evaluating these tumor markers to determine if they can predict how patients might respond to treatment for non-small cell lung cancer.

**Progress:** This protocol was closed to patient entry, 1 Dec 96. No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/116		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9327: Randomized Phase II Pilot Study of Pentoxifylline (Trental) and Placebo in Patients with Metastatic Malignancy and Anorexia/Cachexia Syndrome					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> May 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
			MAJ Richard F. Williams, MC		
LTC Robert D. Vallion, MC			Rakesh Gaur, M.D.		
MAJ John R. Caton, MC					
<b>Key Words:</b> Cancer:metastatic, anorexia,cachexia syndrome, pentoxifylline, placebo					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					//

**Study Objective:** 1) To evaluate the effect of pentoxifylline on the quality of life in patients with anorexia/cachexia syndrome related to malignancy; 2) to evaluate the effect of pentoxifylline on the nutritional status of patients with cancer cachexia and on various laboratory measurements of nutritional status; and 3) to assess the feasibility of accruing patients with cancer cachexia in a cooperative group setting.

**Technical Approach:** The Anorexia/Cachexia Syndrome is a well known entity in patients with metastatic cancer. The mechanism of this entity is felt to be mediated by several factors including cytokine release. Tumor necrosis factor is directly involved in suppressing anabolic enzymes as well as inducing inflammatory and pyrogenic effects by the body. These are all felt to be related to the above syndrome. Pentoxifylline, a TNF inhibitor, has been used in the past for vascular diseases and is well tolerated and will be used in this study to see if any improvement in the anorexia/cachexia syndrome occurs. The end points will be measured by a quality of life questionnaire for both anorexia and fatigue.

**Progress:** No patients have been entered in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/058		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9331 (E2192): Outcome Prediction by Histologic Grading in EST 1180 (SWOG 8294), Ancillary					
<b>Start Date:</b> 02/04/94			<b>Est. Completion Date:</b> Nov 03		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Patrick L. Gomez, MC			MAJ Mark E. Robson, MC		
LTC Robert B. Ellis, MC			MAJ Richard C. Tenglin, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
CPT Diana S. Willadsen, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> cancer:breast, histologic grading					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>02/21/97</b>

**Study Objective:** 1) To evaluate the reproducibility of a combined histopathologic grading system of breast cancer. 2) To evaluate the ability of the grading system to predict time to treatment relapse (TTR) and survival. 3) To use multivariate analyses to evaluate the prognostic importance of the grading data relative to the other clinical and biological factors determined as part of SWOG 8294.

**Technical Approach:** This is a pathology study utilizing the patient set from SWOG 8294. Patients reviewed as part of that study (where cases with adequate specimens for flow cytometry were evaluated and provisionally graded) will be registered to this study. Slides will be reviewed by three investigators and cases will be grouped into 3 prognostic categories. The power calculation for testing the association of this grading system with survival will be based on the "2 degree of freedom" logrank test. The Cox proportional hazards model will also be used in the analysis to adjust the comparisons for effects of other factors.

**Progress:** This study closed to patient accrual 5 Oct 95. Seven patients were enrolled in this study in FY 94 and all are still being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/147		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9333: A Randomized Controlled Trial of Mitoxantrone & Etoposide vs Daunomycin & Cytosine Arabinoside as Induction Therapy in Patients Over Age 55 with Previously Untreated Acute Myeloid Leukemia					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>					
LTC Kenneth A. Bertram, MC			LTC Luke M. Stapleton, MC		
LTC Robert D. Vallion, MC			LTC Robert B. Ellis, MC		
MAJ John R. Caton, MC			MAJ Richard F. Williams, MC		
<b>Key Words:</b> Cancer:leukemia, myeloid, mitoxantrone, etoposide, daunomycin, cytosine arabinoside, over age 55					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		06/21/96	

**Study Objectives:** To compare the complete remission (CR) rate, duration of survival and duration of relapse-free survival (time for CR until relapse or death) for patients aged 56 or older with acute myeloid leukemia (AML) treated with daunomycin (daunorubicin, DNR) and cytosine arabinoside (Ara-C) or with mitoxantrone (Mito) and etoposide. To assess the frequency and severity of toxicities and the durations of neutropenia, thrombocytopenia, and first hospitalization associated with the two induction chemotherapy regimens.

**Technical Approach:** Acute myelogenous leukemia in the elderly population is usually a fatal disease. Although complete remission rates are about 40-60% with standard chemotherapy induction, relapse rates are high and morbid and sometimes fatal toxicities will occur. This multi-center study aims to improve the remission rate and toxicity profile of induction chemotherapy for AML in the elderly using mitoxantrone and VP-16 and comparing it to standard daunorubicin and Ara-C followed by standard consolidation. Colony stimulating factors with GM-CSF will be given prophylactically as well as prophylactic antibiotics with Fluconazole, Ciprofloxacin, and Acyclovir. We expect 3-4 subjects per year and the entire multi-center recruitment is projected to be 100 per year.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/121		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9336: A Phase III Comparison Between Concurrent Chemotherapy Plus Radiotherapy, and Concurrent Chemotherapy Plus Radiotherapy Followed by Surgical Resection for Stage IIIA (N2) Non-Small Cell...					
<b>Start Date:</b> 06/03/94			<b>Est. Completion Date:</b> Jun 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Robert D. Vallion, MC					
<b>Associate Investigators:</b>			COL Daniel G. Cavanaugh, MC		
COL Walter G. Graves, MC			LTC Maceo Braxton Jr, MC		
LTC Blaine R. Heric, MC			MAJ Rahul N. Dewan, MC		
LTC Steven S. Wilson, MC			MAJ Nyun C. Han, MC		
LTC Luke M. Stapleton, MC			LTC Howard Davidson, MC		
LTC Kenneth A. Bertram, MC			MAJ Patrick L. Gomez, MC		
<b>Key Words:</b> Cancer:non-small cell lung, chemotherapy, radiotherapy, surgical resection					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		11/17/95

**Study Objective:** 1) Access whether concurrent chemotherapy and radiotherapy followed by surgical resection results in a significant improvement in progression-free, median, and long-term (2 year, 5 year) survival compared to the same chemotherapy plus standard radiotherapy alone for patients with stage IIIa (N2-positive) non-small cell lung cancer. 2) Evaluate the patterns of local and distant failure for patients enrolled in each arm of the study, in order to assess the impact of the therapy on local control and distant metastases. 3) To obtain exploratory descriptive information on the relationship of tobacco use, alcohol use and dietary patterns on toxicity and outcomes in males and females.

**Technical Approach:** Patients with biopsy-proven Stage IIIa Non-Small Cell carcinoma will be randomized to one of two arms. Arm I and II patients will receive Induction Radiotherapy (45 Gy + concurrent induction chemotherapy (CT) of Cisplatin 50 mg/m<sup>2</sup> IVPB days 1, 8, 29, 36 and VP-16 50 mg/m<sup>2</sup> IVPB, days 1-5, 29-33. Arm I patients will be re-evaluated 2-4 weeks after completion of induction and Arm II will be re-evaluated 7 days before completion of induction. All patients, after re-evaluation, will proceed to Registration 2. If there is no evidence of local progression or distant metastases patients will be assigned options 3 or 4 (Arm I) or option 5 (Arm II). Option 3 consists of surgery plus 2 additional cycles CT starting 4-6 weeks postoperatively, Option 4 of 2 additional cycles CT at least 3 weeks after cycle 2 and Option 5 of continuing RT with no break and beginning 2 additional cycles of CT 3 weeks after cycle 2, day 8. RT boost field will be planned by CT scan. The major endpoints will be median, 2-year and 5-year progression-free and overall survival. Evaluation of patterns of relapse is a secondary endpoint.

**Progress:** Two patients were enrolled in this study (FY 95). Both patients are now deceased.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 95/091	<b>Status:</b> Completed
<b>Title:</b> SWOG 9340: A Phase III Randomized Study of Radiotherapy With or Without BUdR Plus Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Anaplastic Astrocytoma		
<b>Start Date:</b> 03/17/95	<b>Est. Completion Date:</b> Indefinite	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC		
<b>Associate Investigators:</b>		
LTC Howard Davidson, MC	LTC Luke M. Stapleton, MC	
MAJ Timothy P. Rearden, MC	LTC Kenneth A. Bertram, MC	
MAJ James S. D. Hu, MC	LTC Robert B. Ellis, MC	
MAJ Richard F. Williams, MC	LTC Robert D. Vallion, MC	
	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:astrocytoma, radiotherapy, BUdR, Procarbazine, CCNU, Vincristine		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0.00	\$0.00	11/17/95

**Study Objective:** This study will determine if the experimental drug BUdR given before and during radiation therapy, followed by the chemotherapy drugs procarbazine, CCNU, and vincristine can slow the growth of the tumor.

**Technical Approach:** All patients will receive RT and PCV chemotherapy and half will also receive BUdR. Treatment 1) Subject will be given RTX to the brain five days a week for six to seven weeks. Within two weeks after completing RTX, subject will receive CCNU by mouth for one day (day 1 of each cycle). One week later they will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, they will be given vincristine by vein. Subject will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or at least six but no more than eight times) unless the disease worsens or complications arise. Treatment 2) Subject will be given BUdR by vein continuously for 4 days just before starting the first week of radiation therapy and for four days per week starting on day 4 or 15 of RTX each week during the first five weeks of therapy. BUdR will be given either in the hospital or on an outpatient basis. If hospitalization is required, BUdR will be delivered through a vein in the arm. If not hospitalized, BUdR will be delivered by a portable infusion pump through a vein in the neck and shoulder area. Within two weeks after completing RTX and BUdR therapy, the subject will receive CCNU by mouth for one day (day 1). One week later, the subject will be given procarbazine by mouth every day for two weeks (days 8 through 21). On days 8 and 29, the subject will be given vincristine by vein and will continue to receive CCNU, procarbazine, and vincristine every six to eight weeks on this schedule for a period of one year (or for at least six but no more than eight times) unless your disease worsens or complications arise. Blood counts and regularly performed physical examinations and laboratory tests will be taken to measure progress and toxicity from these treatments.

**Progress:** This protocol was closed to patient entry, 14 Apr 97. No patients were entered at MAMC,

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/012		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9347: Phase III Comparison of Tamoxifen versus Tamoxifen with Ovarian Ablation in Premenopausal Women with Axillary Node-Negative Receptor-Positive Breast Cancer < 3cm, Intergroup					
<b>Start Date:</b> 10/20/95			<b>Est. Completion Date:</b> Jul 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
LTC Robert L. Sheffler, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
MAJ John R. Caton, MC					
<b>Key Words:</b> Cancer:breast, Tamoxifen, ovarian ablation, premenopausal					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>OMA Cost:</b>			
\$0		\$0.00		//	

**Study Objectives:** 1) To compare the disease-free survival, overall survival, and toxicity of treatment in hormone receptor-positive, premenopausal women with axillary lymph node-negative breast cancer measuring 3 cm or less given adjuvant therapy with tamoxifen alone, or tamoxifen with ovarian ablation. 2) To obtain tumor tissue from these patients for future biologic studies of relevance to this patient population. 3) To compare menopausal symptoms, sexual function and quality of life in patients receiving tamoxifen alone with patients receiving tamoxifen plus ovarian ablation.

**Technical Approach:** Studies from Scottish trials have shown significant benefit to ovarian ablation for ER receptor positive and lymph node positive breast cancer that are at least as good in terms of overall survival compared to chemotherapy. This study tries to answer this question for patients with less than 3 cm tumors, node negative, ER positive breast cancer patients who are premenopausal. The study has two arms: Tamoxifen vs. Tamoxifen and ovarian ablation. Ovarian ablation will be carried out with either surgical, hormonal or radiation treatment. End points are disease free and overall survival. In addition, tissue will be sent for biologic studies.

**Progress:** No patients entered this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/024		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9349: A Randomized Phase II Trial of CHOP with G-CSF Support or ProMACE-CytaBOM With G-CSF Support for Treatment of Non-Hodgkin's Lymphoma					
<b>Start Date:</b> 11/18/94			<b>Est. Completion Date:</b> Nov 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>					
LTC Howard Davidson, MC			LTC Luke M. Stapleton, MC		
MAJ Timothy P. Rearden, MC			LTC Kenneth A. Bertram, MC		
LTC Robert D. Vallion, MC			LTC Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			CPT Diana S. Willadsen, MC		
			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:Non-Hodgkin's lymphoma, CHOP, ProMACE-CytaBOM, G-CSF					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objectives:** To evaluate the effectiveness of the dose intense CHOP chemotherapy regimen with G-CSF support and the dose intense ProMACE-CytaBOM chemotherapy regimen with G-CSF support in previously untreated patients with intermediate and high grade non-Hodgkin's lymphomas. The effectiveness of the regimens will be based on the estimate of the complete response rate, the time to treatment failure, and ultimately overall survival. To assess the toxicities and side effects associated with the regimens. Also to further utilize the central serum and tissue repositories enabling clinicopathologic correlations with the results of studies on the material collected.

**Technical Approach:** This study attempts to assess whether dose intense CHOP or Promace-CytaBOM with growth factor support will have any effect on improvement of standard first line therapy in non-Hodgkins lymphoma. Ninety-eight patients will be accrued for each of the two arms. This number of patients will allow for both the complete response rate and probability of treatment failure two years after treatment to be estimated to within at most  $\pm 0.10$  for each measure. A successful outcome for either regimen is one that has a true probability of 60% or higher of patients being alive without disease at two years. No formal statistical comparisons between arms will be made.

**Progress:** This protocol was closed to patient entry, 1 Jan 97. Three patients were enrolled in this study in FY 96, and are being followed.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/003		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer					
<b>Start Date:</b> 10/21/94			<b>Est. Completion Date:</b> Oct 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
LTC Robert B. Ellis, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
				<b>11/17/95</b>	

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress:** This study is closed to patient entry 10 Sep 96. One patient was enrolled in FY 96 and is being followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/093		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> CPT Diana S. Willadsen, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Timothy P. Rearden, MC			LTC Robert B. Ellis, MC		
MAJ James S. D. Hu, MC			LTC Robert D. Vallion, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:oligodendroglioma, radiotherapy, CCNU, vincristine, procarbazine, vincristine					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objective:** 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe ( $\geq$  grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.

**Technical Approach:** This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy  $\pm$  PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 94/163		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study					
<b>Start Date:</b> 09/21/94			<b>Est. Completion Date:</b> Sep 98		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> LTC Robert B. Ellis, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
MAJ Timothy P. Rearden, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> cancer:breast, chemotherapy, doxorubicin, Taxol, positive nodes					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		<b>\$0</b>	<b>OMA Cost:</b>		<b>\$0.00</b>
					<b>11/17/95</b>

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** One patient was enrolled at MAMC in FY 97 for a total of eight patients enrolled. Two have expired; six continue to be followed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/094		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9415: Phase III Randomized Trial of 5-FU/Leucovorin/Levamisole versus 5-FU Continuous Infusion Levamisole as Adjuvant Therapy for High-Risk Resectable Colon Cancer, Intergroup					
<b>Start Date:</b> 03/17/95			<b>Est. Completion Date:</b> Feb 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ Timothy P. Rearden, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Howard Davidson, MC			LTC Kenneth A. Bertram, MC		
LTC Robert B. Ellis, MC			MAJ James S. D. Hu, MC		
LTC Robert D. Vallion, MC			CPT Diana S. Willadsen, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:colon, 5-FU, leucovorin, levamisole					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		11/17/95
			\$0.00		

**Study Objective:** To compare the effectiveness of bolus 5-FU, leucovorin, levamisole versus continuous infusion 5-FU, levamisole as adjuvant therapy for patients with Stage B2, C1 or C2 colon cancer. This will be measured in terms of overall survival. Disease-free survival will be a secondary endpoint.

**Technical Approach:** This trial is an intergroup trial involving the Southwest Oncology Group, Eastern Cooperative Oncology Group and the Cancer and Leukemia Group B. Based on previous experience with accrual to INT-0089, and assuming that roughly 1/3 of patients eligible for that study will be entered we anticipate an annual accrual of approximately 600 patients having curative resection of B2, C1, or C2 colon cancer. The primary objective of this study is to compare the survival in patients with high risk resectable colon surgery treated in an adjuvant setting with either 5-FU, leucovorin, levamisole or continuous infusion 5-FU, levamisole. The continuous infusion arm would be judged superior if the true increase in survival is 35%. A secondary endpoint will be disease-free survival. The dose of continuous infusion 5-FU selected for this study of 250 mg/m<sup>2</sup>/d is currently being piloted at an individual institution, and is lower than the common dose of 300 mg/m<sup>2</sup>/d, which required dose reductions in a previous pilot. In order to verify the appropriateness of this dose in the intergroup setting, we will evaluate toxicity and compliance in the first 40 patients randomized to the continuous infusion arm. Should the frequency of dose reductions or toxicities warrant concern, the study may be amended or temporarily closed while the continuous infusion therapy is reassessed.

**Progress:** One patient has been enrolled (FY 97) in this study at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 95/151		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9416: A Phase II Intergroup Trial of Induction Chemoradiotherapy Followed by Surgical Resection for Non-Small Cell Lung Cancer Involving the Superior Sulcus (Pancoast Tumors)					
<b>Start Date:</b> 06/16/95			<b>Est. Completion Date:</b> Jun 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Luke M. Stapleton, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
MAJ John R. Caton, MC					
<b>Key Words:</b> Cancer:non-small cell lung, radiation, cisplatin, VP-16					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					06/21/96

**Study Objectives:** To assess the feasibility and toxicity of treating patients who have pancoast tumors without mediastinal or supraclavicular nodal involvement (T3-4, N0-1) with Cisplatin and VP-16 for two cycle, concurrent with a program of continuous, fractionated chest radiation followed by surgical resection and boost chemotherapy. To assess the objective response rate, resectability rate, and proportion of patients free of microscopic residual disease after such an approach.

**Technical Approach:** This oncology group protocol is a Phase II chemoradiation induction of superior sulcus (pancoast) tumors, non-small cell lung cancer followed by surgical resection. There are no extraordinary requirements of this study. This study should recruit 4-5 MAMC patients a year, 18 or older, and of either sex with selected Stage IIIa (T3, N0-1) or Stage IIIb (T4, N0-1) tumors involving the superior sulcus. The main goals of this study are to estimate the response, toxicity, and resectability rates following the combined chemoradiotherapy. We plan to accrue a total of 99 patients which will allow for estimation of rates and provide a sufficient number which will undergo resection. The precision of estimation of rates within stage IIIA or IIIB will depend on the breakdown by stage.

**Progress:** No patients have been enrolled in this study at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/134		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9419: Tumor Tissue Biopsy for Thymidylate Synthase Expression in Patients with Colorectal Cancer, Ancillary					
<b>Start Date:</b> 08/15/97			<b>Est. Completion Date:</b> Apr 01		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			<b>LTC Robert L. Sheffler, MC</b>		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
Rakesh Gaur, M.D.					
<b>Key Words:</b> Cancer:colorectal, thymidylate synthase					
<b>Accumulative MEDCASE Cost:</b>		<b>\$0</b>	<b>Est. Accumulative OMA Cost:</b>		<b>\$0.00</b>
			<b>Periodic Review:</b>		<b>//</b>

**Study Objective:** 1) To measure thymidylate synthase (TS) expression by polymerase chain reaction in tumor biopsies prior to initiation of fluorinated pyrimidine based therapy in patients with disseminated colorectal cancer and correlate tumor response with level of TS expression; 2) To correlate TS expression in tumor tissue obtained during a potentially curative resection and disease-free survival in patients with Stage II and III large bowel cancer prior to receiving adjuvant therapy with 5-FU based regimen on targeted Southwest Oncology Group trials.

**Technical Approach:** Tissue samples from patients already on other SWOG protocols will be used. These protocols are: SWOG 9250, SWOG 9303, SWOG 9304, SWOG 9415, and SWOG 9420. Patient treatment will not be affected by registration on this protocol. TS expression will be measured using polymerase chain reaction. The following comparisons will be made: The relationship of TS expression (which may be the most important determinant of whether 5-FU will be effective) with tumor response in the disseminated setting and the relationship of TS expression with recurrence free survival in the post-operative adjuvant patients.

**Progress :** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/006	<b>Status:</b> On-going
<b>Title:</b> SWOG 9420: A Phase III Trial of Continuous Low-Dose Infusion Versus Intermittent High-Dose Infusion of 5-Fluorouracil in Patients with Disseminated Colorectal Cancer		
<b>Start Date:</b> 10/18/96	<b>Est. Completion Date:</b> Oct 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
MAJ Richard F. Williams, MC	LTC Robert B. Ellis, MC	
Rakesh Gaur, M.D.	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:colorectal, 5-FU, low dose vs high dose		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

**Study Objective:** 1. To determine whether dose intensity of 5-FU administered for treatment of disseminated colorectal cancer has an impact upon survival 2. Compare response to 5-FU therapy by continuous low-dose versus high-dose intermittent infusion in thymidylate synthase gene expression within metastatic colorectal cancer tumor biopsies.

**Technical Approach:** Metastatic colorectal cancer is incurable. Intervention with chemotherapeutic drugs has shown response rates in the 35 to 50 percent range. Most of these regimens used a biological modulator such as leucovorin in conjunction with 5-FU. Few studies have shown an overall improved survival benefit with chemotherapy compared to observation alone, and in the studies that did show a benefit this prolongation of survival was small. Recently different routes of infusion have been utilized with 5-FU and it is felt that response rates are comparable if not better with continuous infusion as continuous infusion allows perhaps greater total dosage than if given by bolus or it may be related to the greater exposure of drug to tumor in the infusional treatments. This study proposes to compare a treatment incorporating 5-FU by protracted venous infusion compared to high dose weekly infusional 5-FU. The main endpoint is survival. In addition, this study will use data from tumor specimens to correlate Ts gene expression to response rates in the two arms.

**Progress :** Three patients were entered in the study (FY 97) at MAMC. One patient was transferred in from TAMC and ex[ored three months later.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/102	<b>Status:</b> On-going
<b>Title:</b> SWOG 9445: Prognostic Factor Panel to Predict Preferred Therapy for Node Positive Postmenopausal Breast Cancer Patients (CAF vs Tamoxifen) (A Companion Protocol to SWOG 8814)		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> Apr 96	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>	LTC Robert L. Sheffler, MC	
LTC Kenneth A. Bertram, MC	LTC Robert D. Vallion, MC	
MAJ Richard F. Williams, MC	MAJ John R. Caton, MC	
Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:breast, node positive, prognostic factors, CAF, Tamoxifen		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

**Study Objective:** Overall objective is to correlate a panel of markers with clinical outcome and responsiveness to adjuvant therapy of node positive post menopausal breast cancer patients who participated in SWOG 8814. Specifically: 1) To evaluate if c-erbB-2 can allow the discrimination of node positive breast cancer patients who markedly benefited from adjuvant therapy with CAF (those with over-expressed c-erbB-2) from patients who did not obtain additional benefit from dose intensive CAF (those with low c-erbB-2 expression); 2) to measure a panel of prognostic factors (histologic and nuclear grade, estrogen and progesterone receptors, c-erbB-2, p53, Ki67, flow cytometrically determined DNA index and S-phase), angiogenesis, hsp27 (heat shock protein 27), nuclear and histologic grading, and immunohistochemically measured estrogen and progesterone receptors on node positive postmenopausal breast cancer patients; 3) to test the association of the factors listed above with biological and clinical features, including recurrence, survival and apparent efficacy of CAF chemotherapy in patients entered on SWOG 8814; and 4) to cut and store additional sections to allow the evaluation of markers that are mechanistically interesting but in the early development stage in breast cancer prognostic work which may be identified within the next 2-3 years, to be analyzed for prognostic significance and impact on the apparent benefit obtained by adjuvant CAF.

**Technical Approach:** This is a prognostic factor study attempting to find a correlation of several molecular, biochemical, and immunohistochemical, markers with outcomes in node positive breast cancer. It also seeks a correlation of C-erbB-2 expression with benefits of adjuvant chemotherapy compared to tamoxifen therapy alone. The paraffin blocks will be submitted for all patients that are registered on SWOG 8814 who have adequate tissue to submit. It will be submitted to University of Texas Health Science Center in San Antonio, Texas.

**Progress:** Two patients have been entered in this study in previous years. One patient expired in FY 96 and the other is still in follow-up



### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/094	<b>Status:</b> On-going
<b>Title:</b> SWOG 9446: Chemoprevention Trial to Prevent Second Primary Tumors with Low-Dose 13-Cis Retinoic Acid in Head and Neck Cancer		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> Mar 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ John R. Caton, MC		
<b>Associate Investigators:</b>		
LTC Robert L. Sheffler, MC	LTC Luke M. Stapleton, MC	
LTC Robert B. Ellis, MC	LTC Kenneth A. Bertram, MC	
LTC Robert D. Vallion, MC	MAJ James S. D. Hu, MC	
Rakesh Gaur, M.D.	MAJ Richard F. Williams, MC	
<b>Key Words:</b> Cancer:head and neck, 13-Cis retinoic Acid		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

Study Objective: 1) To test the efficacy of prolonged low-dose 13-cRA in reducing the risk of second primary tumors (SPTs) in patients who have had head and neck cancer controlled by surgery and/or radiotherapy; and 2) to evaluate the qualitative and quantitative toxicity of low-dose 13-cRA administered daily for three years.

Technical Approach: Head and neck cancer accounts for 5% of all cancers in the US with 45,000 new cases and 15,000 deaths annually. The standard treatment for early Stage I and II disease is either surgical excision or radiotherapy. However, the major cause of failure in early stage patients is the development of second primary tumors (SPT). The prognosis for patients with SPTs, especially of the lung, is very poor, with a median survival of 5 to 10 months, and less than 10% of patients survive more than 2 years. Toxicity data and the necessity for long-term therapy suggest the need for new chemoprevention approaches to controlling head and neck cancer. Based on recent data showing the greater effectiveness of low dose 13-cRA over B-carotene and mild, tolerable toxicity, we will investigate the efficacy and safety of long-term, low dose 13-cRA for preventing second primary tumors in early stage head and neck cancer.

Progress: No patients have been entered at MAMC.

# Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/117	<b>Status:</b> Completed
<b>Title:</b> SWOG 9449: Phase II Study of VIP (Etoposide, Ifosfamide and Cisplatin) in the Treatment of Invasive Thymoma		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> May 99	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
LTC Robert D. Vallion, MC	LTC Robert B. Ellis, MC	
MAJ John R. Caton, MC	MAJ Richard F. Williams, MC	
	Rakesh Gaur, M.D.	
<b>Key Words:</b> Cancer:thymoma, etoposide, ifosfamide, cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	//

**Study Objective:** 1) To evaluate the objective response rate in extensive thymoma treated with VIP (etoposide, ifosfamide, cisplatin) plus G-CSF; 2) to evaluate the duration of remission and survival in patients with extensive disease treated with VIP plus G-CSF; and 3) to evaluate the toxicity of the VIP regimen in this population.

**Technical Approach:** The overall survival for invasive thymoma is 23 to 80 percent at 5 years. For non-invasive thymoma, the 5 year survival is about 4 times greater. Presently the treatment of invasive thymoma is surgical resection with or without radiation therapy to decrease the recurrence rate. Presently there are no large studies in which to make an inference as to what the standard of therapy should be for invasive thymoma. This study is a phase II single arm study evaluating the effect of a chemotherapy regimen traditionally used for germ cell tumors. The chemotherapy will be given prior to any surgery and a response determination will be made. If a complete remission occurs, then no further treatment will be done. For a partial response, surgical resection will be done if resectable and if stable observation until progression. If any patient has limited disease and is a candidate for resection or xrt, then, they will not be eligible for this protocol. The end points are response rate, duration of response, and overall survival.

**Progress:** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/009		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9457: Paclitaxel (Taxol) and Carboplatin for Advanced Transitional Cell Carcinoma of the Urothelium					
<b>Start Date:</b> 10/18/96			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
MAJ Richard F. Williams, MC			MAJ John R. Caton, MC		
Rakesh Gaur, M.D.					
<b>Key Words:</b> Cancer:urothelium, paclitaxel, carboplatin					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		/ /	

**Study Objective:** 1. To assess the efficacy and feasibility of utilizing a 3 hour infusion of paclitaxel in combination with carboplatin in cases of previously untreated advanced urothelial tract transitional cell carcinoma. 2. To assess efficacy of this regimen with advanced urothelial tract transitional cell carcinoma refractory to platinum-based therapy. 3. To evaluate the toxicity of this regimen in these groups of patients.

**Technical Approach:** Advanced stage urothelial cancer that is not totally resected has a very high relapse rate. In fact in node positive disease it can be argued that these patients are incurable despite local resection. Of course M1 disease is incurable. Standard therapy for these tumors is cisplatin based (MVAC or CMV) with very good response rates in the 50 to 70 percent range. Phase II studies has seen response rates with single agent carboplatin in this range and Taxol single agent response rates in 25 to 30% range. This study is a Phase II study evaluating the efficacy of combined Carboplatin plus Taxol in patients with measurable advanced transitional cell carcinoma of the bladder.

**Progress :** This study was approved in Oct 96. One patient was entered in FY 97.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/059	<b>Status:</b> On-going
<b>Title:</b> SWOG 9503 (NCCTG 93-72-52): Phase III Trial of BCNU and Cisplatin Versus BCNU Alone and Standard Radiation Therapy Versus Accelerated Radiation Therapy in Patients with Grade 4 Glioma		
<b>Start Date:</b> 02/21/97	<b>Est. Completion Date:</b> Feb 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
MAJ Richard F. Williams, MC	LTC Robert B. Ellis, MC	
Rakesh Gaur, M.D.	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:glioma, accelarated radiation therapy, standard radiation, BCNU, cisplatin		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

**Study Objective:** To conduct a 2 x 2 factorial study to compare treatment outcomes in patients with glioblastoma multiforme treated with AHRT (accelerated hyperfractionated radiation therapy) + BCNU + CDDP and those treated with SRT (standard ration therapy) + BCNU + CDDP. Primary goals: 1) To compare the survival distributions of patients treated with AHRT vs patients treated with SRT. 2) To compare the survival distributions of patients treated with BCNU + CDDP before, during, and after radiation therapy vs patients treated with BCNU during and after radiation therapy.

**Technical Approach:** The median survival for patients with high grade gliomas is about 9 to 11 months. The 5 year survival is less than 20% with standard therapy using surgery and radiation therapy. The use of chemotherapy combined with radiation therapy after surgery has shown some small benefit and is considered the standard therapy in most trials. As for radiation therapy, the standard fractionation scheme of 180 cGy has been tested with equivalent results shown in fashion over 15 days (4800 redds total dose). this study will compare 4 treatment Arms using BCNU + standard radiation therapy vs BCNU + accelerated hyperfracti-onation vs BCNU + Cisplatinum and standard radiation therapy vs BCNU + Cisplatinum and accelerated hyperfractionation for high grade gliomas. The toxicity of the two radiation therapy schedules are equivalent and the addition of Cisplatinum to BCNU may radiosensitive with radiation.

**Progress :** No patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/147		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9509: A Randomized Phase III Trial of Paclitaxel Plus Carboplatin Versus Vinorelbine and Cisplatin in Untreated Advanced Non-Small Cell Lung Cancer					
<b>Start Date:</b> 06/21/96			<b>Est. Completion Date:</b>		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
MAJ John R. Caton, MC			Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:Non-small cell lung, paclitaxel, carboplatin, vinorelbine, cisplatin					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
					<b>Periodic Review:</b> 06/20/97

**Study Objectives:** To compare the effect of paclitaxil plus carboplatin to vinorelbine plus cisplatin on overall survival, progression-free survival and tumor response rate in patients with Stage IV and selected Stage IIIB non-small cell lung cancer. To compare the toxicity of the two treatment regimens in patients with Stage IV and selected Stage IIIB non-small cell lung cancer.

**Technical Approach:** The primary objective of this study is to compare the survival in patients with advanced non-small cell lung cancer treated with cisplatin/vinorelbine with that in comparable patients treated with the combination of carboplatin/paclitaxel. Carboplatin/paclitaxel would be judged superior to the standard regimen of cisplatin/vinorelbine if the true increase in median survival is 50%. Based on the previous Group-wide Phase II study in this disease (SWOG ), it is anticipated that 300 total eligible patients per year will be accrued to this study. An accrual period of 16 months should thus result in a study of 200 eligible patients per arm. A median survival of 8 months is anticipated on the cisplatin/vinorelbine. Assuming exponential survival, 16 months of patient accrual, and an additional 12 months of follow-up, a sample size of 200 patients per arm in a study with power 0.94 to detect a 50% increase in median survival in the combination arm, using a one-sided logrank test at level 0.025.

**Progress:** Three patients have been entered at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/041		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9510: Evaluation of Topotecan in Hormone Refractory Prostate Cancer, Phase II					
<b>Start Date:</b> 12/19/96			<b>Est. Completion Date:</b> Dec 00		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>					
LTC Kenneth A. Bertram, MC			LTC Robert L. Sheffler, MC		
MAJ Richard F. Williams, MC			LTC Robert B. Ellis, MC		
Rakesh Gaur, M.D.			MAJ John R. Caton, MC		
<b>Key Words:</b> Cancer:prostate, hormone refractory, topotecan					
<b>Accumulative MEDCASE Cost:</b>		<b>Est. Accumulative OMA Cost:</b>		<b>Periodic Review:</b>	
\$0		\$0.00		/ /	

Study Objective: 1) To evaluate the response (CR and PR only) rate to topotecan in patients with metastatic, hormone-refractory prostate cancer. 2) To assess the qualitative and quantitative toxicities of topotecan administered in a phase II study to patients with metastatic, hormone-refractory prostate cancer.

Technical Approach: Prostate cancer that is refractory to standard first line hormonal manipulations including surgical and chemical orchiectomy has a median survival of about 6 months. The standard of care for hormone refractory prostate cancer is not defined. Response to chemotherapy is poor at about 10 to 15%. This study will assess the response rate and toxicities of Topotecan in hormone refractory prostate cancer patients. The schedule with a 21 day infusion had been tested at New York University and showed only some grade 3 and one grade 4 myelotoxicity. Other side effects are fatigue, nausea, vomiting and diarrhea.

Progress : Three patients were enrolled in this study in FY 97 at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/095		<b>Status:</b> On-going	
<b>Title:</b> SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary..					
<b>Start Date:</b> 04/19/96			<b>Est. Completion Date:</b> May 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
MAJ John R. Caton, MC			Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:breast, lymph nodes, positive receptors, tamoxifen, fenretinide					
<b>Accumulative</b>		<b>Est. Accumulative</b>		<b>Periodic Review:</b>	
<b>MEDCASE Cost:</b>		\$0	<b>OMA Cost:</b>		\$0.00
					/ /

**Study Objective:** 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

**Technical Approach:** The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

**Progress:** One patient as entered in this study in FY 97 at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/118	<b>Status:</b> On-going
<b>Title:</b> SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck		
<b>Start Date:</b> 05/17/96	<b>Est. Completion Date:</b> Jun 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		LTC Robert L. Sheffler, MC
LTC Kenneth A. Bertram, MC		LTC Robert B. Ellis, MC
LTC Robert D. Vallion, MC		MAJ Richard F. Williams, MC
MAJ John R. Caton, MC		Rakesh Gaur, M.D.
LTC Steven S. Wilson, MC		MAJ Nyun C. Han, MC
CPT Brent L. Kane, MC		
<b>Key Words:</b> Cancer:head and neck, surgery, radiotherapy, cisplatinum		
<b>Accumulative</b>	<b>Est. Accumulative</b>	<b>Periodic Review:</b>
<b>MEDCASE Cost:</b> \$0	<b>OMA Cost:</b> \$0.00	//

**Study Objective:** 1) To determine the efficacy of concurrent cisplatinum and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.

**Technical Approach:** In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatinum with concurrent radiation therapy may help in local control. This data comes from *in vitro* as well as *in vivo* data showing cisplatinum may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatinum and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity.

**Progress:** One patient has been entered (FY 96) at MAMC.



# Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 97/005	<b>Status:</b> On-going
<b>Title:</b> SWOG 9518: Phase II Trial of Continuous Topotecan Infusion in Patients with Advanced Soft Tissue Sarcomas		
<b>Start Date:</b> 10/18/96	<b>Est. Completion Date:</b> Sep 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b> <div> LTC Kenneth A. Bertram, MC  MAJ Richard F. Williams, MC  Rakesh Gaur, M.D. </div> <div> LTC Robert L. Sheffler, MC  LTC Robert B. Ellis, MC  MAJ John R. Caton, MC </div>		
<b>Key Words:</b> Cancer:sarcoma, topotecan		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	/ /

Study Objective: To evaluate the response rate of advanced soft tissue sarcoma treated with a prolonged infusion of topotecan, and to define the qualitative and quantitative toxicities of topotecan when administered as a continuous infusion to patients in a cooperative setting

Technical Approach: The most active agents for advanced soft tissue sarcomas are DTIC, Adriamycin, Ifosfamide however, improvements in response are needed in the form of newer agents. Topotecan is a Topoisomerase I inhibitor that has been used in non small cell lung cancer studies and its main toxicity is diarrhea, thrombocytopenia, and neutropenia. In this phase II study, Topotecan will be given on a continuous infusion shcedule to assess what the response rate may be with this agent in the hopes of increasing the response rate in soft tissue sarcoma.

Progress : No patients have been enrolled in this study as MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 96/160	<b>Status:</b> Suspended
<b>Title:</b> SWOG 9519: Evaluation of Tomudex in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck		
<b>Start Date:</b> 09/20/96	<b>Est. Completion Date:</b> Aug 00	
<b>Department:</b> SWOG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC		
<b>Associate Investigators:</b>		
LTC Kenneth A. Bertram, MC	LTC Robert L. Sheffler, MC	
MAJ Richard F. Williams, MC	LTC Robert B. Ellis, MC	
Rakesh Gaur, M.D.	MAJ John R. Caton, MC	
<b>Key Words:</b> Cancer:Head and neck, tomudex		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$0.00	05/16/97

**Study Objective:** 1) To evaluate the response rate of histologically confirmed recurrent or metastatic squamous cell carcinoma of the head and neck following Tomudex treatment, in order to assess whether Tomudex should be advanced to further studies; and 2) to assess the qualitative and quantitative toxicities of Tomudex.

**Technical Approach:** Recurrent and metastatic head and neck cancer is incurable. Response rates with chemotherapy have varied, but range from 30 to 75 percent. These response rates are usually not durable and will usually progress within less than 6 months. Chemotherapeutic agents used are cisplatin and 5 FU alone or in combination, methotrexate, and bleomycin. Tomudex is a new agent that is a specific thymidilate synthetase inhibitor. 5 FU is a TS inhibitor but is non-specific. Tomudex has been used in North America and European trials in colorectal cancer and has shown about a 30 percent response rate. Tomudex will therefore be used to assess its response rate and duration of response in a Phase II trial. The main side effects are diarrhea and cytopenia (especially leukopenia), and reversible liver function test abnormalities.

**Progress:** One patient in Sep 96 and died of disease in Oct 96

### Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 96/119		<b>Status:</b> Suspended	
<b>Title:</b> SWOG 9520: Controlled Phase II Study of Doxorubicin and Paclitaxel as Frontline Chemotherapy for Women With Metastatic Breast Cancer					
<b>Start Date:</b> 05/17/96			<b>Est. Completion Date:</b> Apr 99		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b>			LTC Robert L. Sheffler, MC		
LTC Kenneth A. Bertram, MC			LTC Robert B. Ellis, MC		
LTC Robert D. Vallion, MC			MAJ Richard F. Williams, MC		
MAJ John R. Caton, MC			Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:breast, doxorubicin, paclitaxel					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		05/16/97

**Study Objective:** 1) To evaluate the complete remission rate of the doxorubicin plus paclitaxel combination in advanced breast cancer patients with no prior chemotherapy for metastatic disease and either no prior adjuvant chemotherapy or one prior adjuvant chemotherapeutic regimen (non-anthracycline or taxane containing). This evaluation will be made over six cycles of the combination regimen. 2) To test the combination of doxorubicin and paclitaxel for toxicity with particular emphasis on the degree of myelosuppression and the possible cardiac toxicity.

**Technical Approach:** Metastatic breast cancer is an incurable disease with median survivals of approximately 18 months being reported in many trials. The biologic behavior is very heterogeneous and differences in survival can be seen from study to study. Presently adriamycin-based chemotherapy regimens have shown the most efficacy in terms of response rates, however, long term survivals are the exception. Taxol has shown to have significant activity in metastatic breast cancer and has been combined with adriamycin to treat metastatic breast cancer in single arm trials. Evaluations in this study will be done in conjunction with a concurrently randomized control arm (of doxorubicin and cyclophosphamide) which will be used mainly to assess whether the new regimen has been tested in a patient population with historically expected rates of complete remission and congestive heart failure. This evaluation will be made over six cycles of the combination regimen. Because of the incidence of cardiac toxicity with the Milan regimen, close follow-up of cardiac function will be done in all patients in this trial with maximum doses of Adriamycin to be held well below the threshold of 450 mg/m<sup>2</sup>.

**Progress:** No patients have been entered at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97		<b>Protocol no.:</b> 97/070		<b>Status:</b> On-going	
<b>Title:</b> SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour ....					
<b>Start Date:</b> 03/21/97			<b>Est. Completion Date:</b> Mar 00		
<b>Department:</b> SWOG			<b>Facility:</b> MAMC		
<b>Principal Investigator:</b> MAJ James S. D. Hu, MC					
<b>Associate Investigators:</b> LTC Robert B. Ellis, MC MAJ John R. Caton, MC			LTC Robert L. Sheffler, MC MAJ Richard F. Williams, MC Rakesh Gaur, M.D.		
<b>Key Words:</b> Cancer:Non-small cell lung, Vinorelbine, Cisplatin, Observation alone, Tumour Markers					
<b>Accumulative MEDCASE Cost:</b>		\$0	<b>Est. Accumulative OMA Cost:</b>		\$0.00
			<b>Periodic Review:</b>		//

**Study Objective:** 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.

**Technical Approach:** The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation.

In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.

**Progress :** No patients have been entered at MAMC.

DETAIL SHEETS FOR PROTOCOLS

UNIVERSITY OF WASHINGTON NEURO-  
ONCOLOGY

## Detail Summary Sheet

<b>Date:</b> 30 Sep 97	<b>Protocol no.:</b> 89/013	<b>Status:</b> On-going
<b>Title:</b> UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System		
<b>Start Date:</b> 01/20/89	<b>Est. Completion Date:</b> Nov 92	
<b>Department:</b> UWNG	<b>Facility:</b> MAMC	
<b>Principal Investigator:</b> LTC Howard Davidson, MC		
<b>Associate Investigators:</b> Edythe A. Albano, M.D. MAJ Frank A. Zimba, MC CPT Denis Bouvier, MC MAJ Everardo E. Cobos Jr., MC		Robert Goodkin, M.D. MAJ Joseph H. Piatt, MC COL Irwin B. Dabe, MC MAJ Mark H. Kozakowski, MC LTC Kenneth A. Bertram, MC
<b>Key Words:</b> lymphoma:central nervous system,chemoradiotherapy,methotrexate		
<b>Accumulative MEDCASE Cost:</b>	<b>Est. Accumulative OMA Cost:</b>	<b>Periodic Review:</b>
\$0	\$328.00	12/17/93

**Study Objective:** To evaluate this regimen, the end-points of analysis will be: time to progression of disease from beginning of therapy, response rates and disease stabilization rates, survival time measured from the beginning of therapy, quality of life, and activity level measured by Karnofsky performance status.

**Technical Approach:** Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver function, and a performance status of >70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m<sup>2</sup>, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses, parenterally, on an every 6 hour basis, following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time, the patient will be removed from the protocol and can be treated with other therapy as indicated. Patients will be followed until death.

**Progress:** The protocol has been closed to patient entry. One patient was enrolled and is still being followed.

## NAMES

Adams NR 3  
 Addy C 2  
 Ainbinder DJ 6  
 Albano EA 611  
 Alderman BW 156  
 Aldous WK 1, 2, 73, 74, 75, 76, 81, 82, 223, 298,  
     299, 300, 301, 302, 370, 371, 372  
 Alsarraf R 361  
 Andary M 267  
 Andersen CA 393, 394  
 Anderson FD 4, 219, 220  
 Anderson RH 2, 212  
 Apodaca C 248, 252  
 Arendt MA 136, 137, 138, 139, 140, 141, 142,  
     146, 148  
 Armondo AA 4, 211  
 Armstrong AY 249  
 Armstrong PJ 394  
 Arnold BF 252  
 Aro J 89  
 Asato AJ 94  
 Azarow KS 6, 9, 300, 301, 302, 315, 316, 363,  
     364, 365  
 Babu SS 2, 3, 501  
 Bach A 121  
 Bae VL 10  
 Baechler VR 255  
 Bagg MD 389, 527, 557  
 Baker TM 511, 512, 513, 514, 515, 516, 517,  
     518, 519, 520, 521, 522  
 Baker TP 83  
 Bal GK 7, 336, 337, 338, 339, 340, 341, 349  
 Balser J 371  
 Bandrowsky T 1, 102  
 Banner HM 230  
 Barfield W 263  
 Barfield WA 6  
 Barker AJ 3, 133  
 Barrett JP 3, 133  
 Bauer AJ 262  
 Bauman JM 124, 282, 283, 287  
 Beachy JC 86, 222, 232, 258  
 Beaver GW 193  
 Behrens ML 4  
 Bell BK 302  
 Bell DE 106  
 Bell M 6, 275  
 Belville WD 511, 518  
 Bender GN 5, 6, 7, 155, 284, 289, 291, 293, 303  
 Benirschke SK 7  
 Benson PJ 121  
 Benson WL 400, 401, 404, 405, 406, 407, 408,  
     409, 410, 412, 413  
 Berry DL 6, 10, 380, 381  
 Berry KH 266  
 Berry S 3  
 Berry TR 4  
 Bertram KA 1, 160, 161, 162, 163, 164, 165,  
     166, 167, 168, 169, 170, 171, 175, 176,  
     177, 290, 460, 489, 490, 523, 525, 526,

527, 529, 530, 531, 532, 533, 536, 537,  
 538, 539, 543, 544, 545, 546, 548, 549,  
 550, 551, 553, 554, 555, 557, 558, 559,  
 560, 561, 562, 563, 564, 565, 566, 567,  
 568, 570, 571, 572, 573, 574, 575, 576,  
 577, 578, 579, 580, 581, 582, 583, 584,  
 585, 586, 587, 588, 589, 590, 591, 592,  
 593, 594, 595, 596, 597, 598, 599, 600,  
 601, 602, 603, 604, 605, 606, 607, 608,  
 611  
 Beverly CS 242  
 Bevill KL 307  
 Bianchi AM 92, 210  
 Biglow MV 129  
 Billingsley J 124, 282, 283  
 Birgenheier PS 5, 223, 237  
 Blackburn ST 224, 232, 233  
 Blakeslee DB 520  
 Blanchard JR 203  
 Blanton CL 8  
 Blaser JL 310  
 Block P 354  
 Blumenstein BA 6, 10  
 Boam WD 2  
 Bolger B 358  
 Bolt JL 194, 195  
 Bolt SL 71  
 Borris TJ 1, 102  
 Bouvier DP 518, 523, 524, 525, 526, 528, 529,  
     530, 533, 536, 537, 538, 543, 611  
 Boyko EJ 156  
 Bradshaw DM 132  
 Brantner RD 104, 105, 108  
 Braxton M 296, 586  
 Brazelo MB 334  
 Brencick M 280  
 Brissette MD 5, 172, 345  
 Brown AW 510  
 Brown FB 240  
 Brown FE 248  
 Brown SR 283  
 Brown TA 2, 298, 299, 300, 301, 302, 303  
 Brown Z 3  
 Browne M 397  
 Bryson DR 512, 515, 516, 517, 519, 520, 521,  
     522  
 Buettner M 117  
 Buller JL 4, 240, 241, 377  
 Bullock JM 2  
 Burke LC 266  
 Burke TF 1, 106, 113, 114  
 Burri BJ 69  
 Bush WH 5  
 Bute BG 242  
 Butler R 111  
 Byrne RA 255, 277, 279  
 Cadiz JL 531, 532, 535, 539, 540, 541, 544,  
     545, 546, 547, 548, 549, 550, 552, 555,  
     558, 559, 561, 562, 563, 564, 566, 568,  
     571, 572, 573  
 Caldwell SC 85  
 Calhoun BC 156, 239, 245, 246, 248, 250, 252,  
     253

Cambier PA 2, 3, 136, 137, 144, 145, 146, 147, 188  
 Campbell CS 4, 6  
 Cannon CP 342  
 Caras WE 198, 200  
 Carpenter CT 6, 342, 343, 344  
 Carrougher JG 154, 157, 158, 190  
 Carstens J 145  
 Carter ER 4, 256, 257, 259, 260, 264  
 Carter PL 2, 3, 304, 307, 314, 315, 316, 501  
 Carter SL 83  
 Cartwright VW 257, 260  
 Carver TD 114, 262  
 Casey RL 249  
 Casha LM 6, 285  
 Caton JR 161, 162, 166, 168, 171, 173, 175, 176, 460, 489, 490, 551, 554, 560, 565, 570, 574, 577, 580, 583, 585, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609  
 Cavanaugh DG 215, 547, 586  
 Cawthon MA 5  
 Chambers SE 233  
 Chamusco RF 136, 137, 140, 142, 146  
 Chan AH 511, 513  
 Chan CC 6  
 Chapin BL 2  
 Chapman JB 4, 211  
 Chapman JR 7  
 Charette JD 107  
 Cheever MA 382  
 Chismire KJ 8, 319, 320, 323  
 Chooljian D 357  
 Chrousos GP 88  
 Chun BB 7, 8, 321, 322, 329  
 Chun GG 328  
 Chun YH 122  
 Chung MH 305, 306  
 Clagett CL 200  
 Clark JB 2, 123, 125  
 Clark SJ 4, 214, 226  
 Claudi B 7  
 Clifford AJ 69  
 Cline AD 270  
 Cobb GA 218  
 Cobos E 523, 526, 529, 530, 531, 532, 533, 535, 536, 537, 538, 539, 540, 541, 543, 547, 552, 611  
 Collier HE 2, 136, 137, 145, 146  
 Collins DM 191, 199, 393  
 Colman LK 516, 517, 518, 519, 522  
 Congdon JE 513  
 Contreras M 5  
 Cook BA 463, 464, 465, 466, 467, 468, 469, 470, 471, 473, 474, 475, 476, 477, 478, 479, 481, 482, 485, 493, 494  
 Cooper RH 106, 179, 189  
 Coppola M 111  
 Corey L 3  
 Corn B 7  
 Cote MG 124, 151  
 Coughlin WF 8, 327

Coyle LC 145  
 Cragun WH 199, 205, 394  
 Crane L 98  
 Creedon FA 89  
 Crocker JD 287  
 Crothers BA 501  
 Crouch DN 3  
 Cruess DF 7  
 Cummings P 275  
 Curry TK 90, 315, 316  
 Dabe IB 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 524, 525, 528, 538, 611  
 Dahlgren T 109  
 Dahlhauser KF 8, 9, 319, 320, 333  
 Daniels JL 2, 3, 304  
 Davidson H 160, 166, 460, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 555, 567, 558, 559, 560, 561, 562, 563, 564, 567, 570, 571, 572, 573, 574, 575, 576, 578, 579, 580, 581, 582, 584, 586, 587, 589, 590, 591, 592, 593, 611  
 Davies T 351  
 Davis BJ 305  
 Davis GD 4, 5, 6, 210, 240, 241, 242, 243, 244, 248, 269, 377  
 Davis RC 523  
 Deaconson TF 308, 314  
 Debo RF 357, 366  
 Decker LA 2, 3, 240, 241, 248  
 Decker MJ 390  
 Delaney JW 256  
 Delaplain CB 2  
 Della-Giustina DA 105  
 DePaul D 4, 5, 219, 223, 228, 233  
 DeQuattro N 4  
 Dettori JR 270, 271  
 DeVine JH 6  
 Dewan RN 524, 546, 552, 586  
 Dietz JW 344  
 Dillard TA 3, 198, 200, 202, 204, 394  
 Dillingham TD 267  
 Disis N 382  
 Divelbiss BJ 4  
 Do NV 150, 151, 152  
 Dombroski RT 92, 124, 348  
 Dougherty RW 353  
 Downey GO 405, 408  
 Drotts DL 1, 108  
 Dunning DM 517, 518, 519, 522  
 Dyer RE 235  
 Dyster M 7  
 Edmond CV 9, 357, 358, 360  
 Edmonds DJ 3  
 Edson T 328  
 Eggebrotten WE 307, 308, 314, 315, 316  
 Eisenhauer MD 2, 136, 137, 140, 145, 146, 148, 191



Eisenhower TL 2, 145  
 Elliott MA 3  
 Ellis J 233  
 Ellis RB 160, 161, 166, 167, 168, 169, 171, 172,  
     173, 174, 175, 176, 460, 489, 490, 531,  
     532, 535, 539, 540, 541, 544, 545, 546,  
     547, 548, 549, 550, 551, 552, 553, 554,  
     555, 558, 559, 561, 562, 563, 564, 565,  
     566, 567, 568, 570, 571, 572, 573, 574,  
     575, 576, 577, 578, 579, 580, 581, 582,  
     583, 584, 585, 587, 588, 589, 590, 591,  
     592, 593, 594, 595, 596, 598, 599, 600,  
     601, 602, 603, 604, 605, 606, 607, 608,  
     609  
 Ellis WJ 6, 10, 380  
 Ellsworth C 280  
 Ellsworth JB 368, 377, 378, 388  
 Esplin VS 347  
 Etzkorn ET 106  
 Evans KC 377  
 Evans P 3, 130  
 Evans RK 129  
 Fairchok MP 114, 258, 264  
 Fajardo ET 155  
 Falcon C 106  
 Fannin LA 327  
 Faucette KJ 462, 463, 464, 465, 466, 467, 468,  
     469, 470, 471, 472, 473, 474, 475, 476,  
     477, 478, 479, 480, 481, 482, 484, 485,  
     486, 487, 488, 489, 490, 491, 492, 493,  
     494, 495, 496, 497, 498, 499  
 Fawcett D 358  
 Feber KM 10, 369  
 Feider LL 212  
 Fiaschetti DK 101  
 Fincher RK 155, 181, 182, 183  
 Finney NS 152  
 Fisher LD 361  
 Fleet SJ 188  
 Flynn DM 125  
 Flynn M 128  
 Foley JP 371  
 Foley KS 262  
 Forsythe MA 213  
 Frei DF 6  
 Frohna WJ 115  
 Fuller F 109, 110, 116  
 Fuller GM 231  
 Gagliano RA 364, 365  
 Gagnon-Bailey S 202  
 Gallucci BJ 227, 231  
 Games J 66  
 Garner D 7  
 Gates GA 361  
 Gatlin BD 250  
 Gaur R 161, 162, 163, 164, 165, 168, 170, 171,  
     175, 176, 177, 554, 565, 583, 595, 596,  
     597, 598, 599, 600, 601, 602, 603, 604,  
     605, 606, 607, 608, 609  
 Gayle EL 2  
 George DP 8, 327  
 George RK 6, 319, 320, 323  
 Gerlock AA 396  
 Gernon WJ 520  
 Giacoppe GN 201, 203  
 Gibbons JL 259  
 Gibbons RV 3, 184  
 Gibson R 326  
 Gielen AC 398  
 Gilbert BN 8  
 Gilbert G 324  
 Gillett J 144  
 Gilliam LS 243  
 Gitter A 267  
 Glover WD 222  
 Godwin JD 5  
 Goeken AFW 99, 348  
 Goldman DP 6  
 Goldschlager N 143  
 Gomella LG 7  
 Gomez PL 160, 166, 460, 523, 526, 527, 529,  
     530, 531, 532, 533, 535, 536, 537, 539,  
     540, 541, 543, 544, 545, 546, 547, 548,  
     549, 550, 552, 553, 555, 557, 558, 559,  
     560, 561, 562, 563, 564, 566, 567, 568,  
     571, 572, 573, 575, 576, 577, 578, 579,  
     581, 582, 584, 586  
 Gomez RR 1, 282, 389  
 Gonzales J 354  
 Goodkin R 611  
 Goodman B 145  
 Gower WR 2  
 Grabill NR 1  
 Grathwohl KWA 3, 4, 200, 202, 203, 206, 226  
 Graves WG 586  
 Grazko MB 9, 320  
 Greefkens SE 255  
 Gries DM 6, 259  
 Griffin DE 73, 106  
 Grover BS 205  
 Gunzenhauser J 6  
 Gunzenhauser JD 5, 125, 132, 273  
 Gupta KL 6  
 Hadley SC 324  
 Haggerty MF 5  
 Haig A 267  
 Haik BG 6  
 Halper J 113  
 Hamblen E 91, 99, 348, 354  
 Han NC 172, 290, 565, 586, 605  
 Hanaford B 358  
 Hanny L 7  
 Hansberry KL 7, 10, 381, 383, 384, 391, 527,  
     557  
 Hansen BR 309, 315, 316  
 Hansen EA 7, 8, 319, 320, 329  
 Harrell L 183  
 Harrington BC 3  
 Harris MD 2, 126  
 Hassid EI 196  
 Hauger FH 127  
 Hawkinson R 351  
 Heath GW 2, 77  
 Hecker L 154  
 Heiner SL 214, 215, 216  
 Heitkemper MM 214

Helman JD 71  
 Henderson SR 7  
 Henley MB 7, 336  
 Herd M 247  
 Heric BR 145, 148, 215, 296, 586  
 Hermann-Do KA 99, 354  
 Hibbert ML 4, 240, 241  
 Hicks KA 138, 139, 140, 141  
 Higano CS 174  
 Hildebrand RK 345, 346  
 Hildreth PJ 215, 217, 218, 221  
 Hill C 1, 2, 99  
 Hill E 3  
 Hinson RM 4, 114, 252, 260, 261, 262, 263  
 Ho VB 5, 8, 327, 501  
 Hodges GF 562  
 Hoeldtke NJ 239, 245, 246, 250, 252, 253, 262  
 Hoffman JR 111  
 Holland RM 363, 462, 491  
 Holt CP 2, 3, 304, 501  
 Homann JF 541, 547  
 Horne TA 138, 141  
 Hornstein EH 187  
 Horwhat JD 3  
 Hu JSD 160, 161, 162, 166, 167, 168, 169, 171,  
     175, 176, 460, 489, 490, 532, 539, 544,  
     545, 546, 548, 549, 550, 551, 553, 554,  
     555, 558, 559, 560, 561, 562, 563, 564,  
     565, 566, 567, 568, 570, 571, 572, 573,  
     574, 575, 576, 577, 578, 579, 580, 581,  
     582, 583, 584, 585, 587, 588, 589, 590,  
     591, 592, 593, 594, 595, 596, 597, 598,  
     599, 600, 601, 602, 603, 604, 605, 606,  
     607, 608, 609  
 Huchun A 6  
 Hume RF 125, 156, 245, 246, 247, 248, 252,  
     253  
 Hunter BP 4, 211  
 Hunter GJ 5  
 Hurley WT 106  
 Hyder AE 235  
 Imbruglio LR 233  
 Inglis A 362  
 Inouye L 3  
 Jackson JL 3, 183, 184, 185, 186, 187  
 James SB 250  
 Jarrett RV 114  
 Jarvik G 156  
 Jennings BLM 3, 4, 217, 219, 220, 221  
 Johnson B 2  
 Johnson BR 126, 129  
 Johnson R 89  
 Johnstone FL 345, 347  
 Jones DEC 91, 121, 244, 337, 347, 348, 349,  
     351  
 Jones KW 8  
 Jones MP 165, 170  
 Jones RE 2  
 Jones RJ 3  
 Jordan RA 184  
 Jorden TV 7  
 Jung CJ 361  
 Kambiss SM 4, 251

Kanar E 393  
 Kane BL 165, 290, 565, 605  
 Kane C 371  
 Kanne TJ 9, 359  
 Kao CC 2  
 Kao TC 7  
 Kapur V 207  
 Karge W 2  
 Karstetter KW 1  
 Katakhar SB 508, 509  
 Kavolius J 301, 302  
 Keene CA 2  
 Kelly BJ 92  
 Kelly PC 114, 255  
 Kennedy TE 3  
 Kern JD 207  
 Kiesling VJ 518  
 Killien MG 233  
 Kim DG 305, 308  
 Kim NW 371, 373  
 Kimmey MB 154  
 King JJ 138, 141  
 Kirk ME 352  
 Knight RW 7  
 Knodel DH 2  
 Kopelman JN 3, 247, 251, 262  
 Kortepeter M 5  
 Kowdley KV 154  
 Kozakowski MH 523, 525, 526, 529, 530, 533,  
     536, 537, 538, 543, 611  
 Kransdorf MJ 6, 285  
 Krauss MR 5, 6, 73, 274, 275  
 Kristal AR 385  
 Krober MS 258  
 Kroenke K 3  
 Krolicki TJ 319, 320, 330  
 Kruse RW 344  
 Kubis KC 8  
 Kugler JP 3  
 Kull DH 410  
 Kumar SJ 4, 129, 267, 268  
 Kungys AS 91  
 Kyle DE 75  
 Ladd RC 124  
 Ladwig ML 248  
 Lambie MG 277  
 Lampe J 385  
 Lancaster AK 125  
 Lance RS 7, 10, 298, 299, 302, 310, 311, 370,  
     371, 372, 373, 374, 377, 378, 384, 386,  
     388  
 Landry FJ 203  
 Langston A 173  
 Larsen FW 250  
 Lauder TD 4, 6, 8, 267, 268, 269  
 Lavieri-Reynolds CA 104  
 Leander DJ 222  
 LeClerc KM 3, 138, 139, 140, 141, 148, 188  
 Lee RB 400, 401, 404, 405, 406, 407, 408, 409,  
     410, 412, 413, 517  
 Lee SP 156  
 LeMar HJ 2, 150, 151, 152  
 Lentz MJ 233

Lesho EP 189  
 Lester KS 278  
 Lilliam L 244  
 Linskens P 67  
 Loan LA 4, 213, 214, 215, 216, 217, 219, 220,  
 221, 222, 223, 224, 225, 228, 233, 236  
 Lombardi W 5  
 Low LL 203  
 Lutz RH 109, 118  
 Lynch S 371  
 Lyons MF 155, 282, 284  
 MacDonald DC 2, 130  
 Macri CJ 4  
 Maddison L 10  
 Mader TH 6, 7, 8, 9, 319, 320, 321, 324, 325,  
 326, 327, 328, 331, 333  
 Mafee MF 6  
 Magelssen DJ 249  
 Magruder CD 398  
 Mais DD 309  
 Makuch RS 5, 6, 287  
 Mallory PL 242  
 Mancuso JJ 250  
 Mansfield LT 5, 7, 288  
 Marcantoni HW 1, 102  
 Marden LA 1, 2, 92, 93, 94  
 Markenson GR 5  
 Marshall RC 128  
 Martin DC 129  
 Martin RK 9, 74, 75, 360  
 Martin T 301, 302  
 Martinez CH 64  
 Mascette AM 3, 110, 136, 137, 138, 139, 140,  
 141, 142, 145, 146  
 Maslow AS 3, 262  
 Masson JR 279  
 Matej LA 1, 2, 78, 82  
 Matheson EJ 256  
 May EF 3, 6, 8, 9, 193, 319, 320, 332, 334  
 Mays RA 397, 398  
 Mazzoli RA 6, 7, 8, 319, 320, 322, 327, 329  
 McBiles M 5  
 McCarthy MS 4, 212, 226  
 McClellan DR 79, 257  
 McCllure G 240  
 McDonald JM 83, 303, 310  
 McEwen AK 239  
 McFarland M 357  
 McHenry JA 136, 140, 143, 146  
 McIlmail D 107  
 McLean D 7  
 Meier CM 3  
 Mesaros GJ 9, 360  
 Meyer CA 3, 5, 191, 286  
 Meyer G 3  
 Meyer K 377  
 Michaud MJ 97  
 Migala AF 119  
 Milczuk H 6  
 Miller BJ 71  
 Miller MA 117  
 Miller RC 4  
 Miller RI 277  
 Miller SE 138, 139, 140, 141, 144  
 Miller TH 227, 231  
 Millien MG 228  
 Miser WF 2, 3, 130, 132  
 Mitchell GT 396  
 Mitchell PH 217, 221  
 Mittelstaedt EA 228  
 Mittendorf R 261  
 Mode D 7  
 Moffitt DR 4, 256, 259  
 Moinpour CM 6, 10  
 Mooneyham RD 7  
 Moore CJ 4, 211, 229  
 Moore DC 79, 80, 88  
 Moore KH 1, 2, 81, 82, 83, 84, 156, 172, 253,  
 262, 310, 374  
 Moore RW 257  
 Morgan ED 131  
 Morgan RE 289  
 Morissette JC 7, 294  
 Moritz P 3  
 Morris J 128, 181  
 Morris JT 106  
 Morris MR 536  
 Moss MT 3  
 Moul JW 7, 371, 387  
 Moureau PM 230, 231  
 Murphy GP 374  
 Murray TR 4, 105, 200, 202, 204, 206  
 Myers JB 300  
 Mygrant BI 215, 216, 218  
 Nace MC 249  
 Neill GF 4  
 Nelson KM 261  
 Nelson ML 7, 8, 321, 322, 328, 329  
 Nessel MJM 84  
 Newman RJ 80  
 Newmark J 3, 196  
 Ng JD 8  
 Nguyen PL 5  
 Niebuhr DW 6, 274  
 Nielsen RE 6, 9, 85, 342, 355  
 Nieman D 67  
 Niemeyer DM 2  
 Noble 89  
 Noonburg GE 350  
 Norbeck JC 377, 384, 388, 527, 557  
 North J 301, 302  
 Norton S 361  
 Norvell DC 271  
 Norwood A 397  
 Nussenblatt RB 6  
 O'Bryant LK 6, 9, 364, 365  
 O'Campo PJ 398  
 O'Reilly KJ 370, 374, 375, 376, 377, 388  
 O'Rourke TJ 511, 513, 514, 515, 520, 521  
 Offner PJ 306, 307, 308, 309, 314, 317  
 Olsen SB 393, 394  
 Olson J 142, 146, 148  
 Olson JP 136, 137, 138, 139, 140, 141, 145  
 Osgard EM 3, 188, 190  
 Ostrander E 173  
 Otlege J 3

Pace SA 1, 2, 3, 92, 107, 110, 112, 113, 114,  
 115, 116, 117  
 Palacia PE 4  
 Palmer SR 462, 463, 464, 465, 466, 467, 468,  
 469, 470, 471, 472, 473, 474, 475, 476,  
 477, 478, 479, 480, 481, 482, 484, 485,  
 486, 487, 488, 489, 490, 491, 492, 493,  
 494, 495, 496, 497, 498, 499  
 Palowski RJ 89  
 Parmley VC 8, 9, 143, 319, 320, 321, 324, 325,  
 327, 328, 331, 333  
 Patience TH 2, 3, 9, 86, 256, 298, 299, 324, 334,  
 370, 372  
 Pavlin JA 273  
 Payne C 122  
 Peele ME 137  
 Peller TP 155, 284  
 Peniston J 5  
 Perez RP 4, 240, 241  
 Perkins JA 6, 9, 359, 361, 362, 363, 364, 365  
 Perkins TA 258  
 Peroutka SJ 3, 8  
 Peterson AC 7, 311  
 Petroski RA 7, 375, 376  
 Pezzin LE 267  
 Phillips WA 531, 540, 541, 547  
 Phyll G 4, 6  
 Piatt JH 611  
 Pierce HI 503, 504, 505, 506, 507, 508  
 Pierce RH 2  
 Pierson DM 215  
 Pike JD 203  
 Pina JS 4, 5  
 Pitcher JD 5, 6, 7, 288, 292, 312, 313, 341, 346,  
 351  
 Place RJ 307  
 Plymate SR 10, 385, 389  
 Poffenbarger GJ 66  
 Polse KA 8  
 Pontius D 235  
 Poore SE 4  
 Porter CA 302, 308, 314, 315, 316  
 Potter H 353  
 Potter ME 248, 249, 400, 401, 402, 403, 404,  
 405, 406, 407, 408, 409, 410, 411, 412,  
 413, 414, 415, 416, 417, 418, 419, 420,  
 421, 422, 423, 424, 425, 426, 427, 428,  
 429, 430, 431, 432, 433, 434, 435, 436,  
 437, 438, 439, 440, 441, 442, 443, 444,  
 445, 446, 447, 448, 449, 450, 451, 452,  
 453, 454, 455, 456, 457, 458  
 Powell JB 94, 280  
 Pulos E 9, 217, 221, 228  
 Pusateri A 270  
 Qabar AN 2, 74, 87  
 Quinn KL 208  
 Raiha NK 6, 275, 397, 398  
 Ramakrishna R 200  
 Ramayya MS 88  
 Rand RP 2  
 Rave MA 137  
 Rawlings JS 258  
 Raymond WR 7, 8, 257, 319, 320, 329  
 Rearden TP 160, 174, 460, 527, 544, 548, 551,  
 553, 555, 557, 560, 561, 564, 566, 567,  
 568, 570, 571, 572, 573, 574, 575, 576,  
 577, 578, 579, 580, 581, 582, 584, 587,  
 589, 590, 591, 592, 593  
 Reddoch SE 462, 463, 464, 465, 466, 467, 468,  
 469, 470, 471, 472, 473, 474, 475, 476,  
 477, 478, 479, 480, 481, 482, 484, 485,  
 486, 487, 488, 489, 490, 491, 492, 493,  
 494, 495, 496, 497, 498  
 Reece WB 165  
 Reed HL 150, 151, 152  
 Regan NA 204, 206  
 Rembold JM 4  
 Renaud MT 4, 5, 232, 233  
 Rich L 321  
 Richardson MA 6  
 Riggins JW 324  
 Riley ME 234  
 Rivara F 6, 275  
 Robson L 1, 2, 92, 93, 94, 95, 99, 354  
 Robson ME 160, 166, 460, 544, 548, 553, 555,  
 560, 561, 564, 566, 567, 568, 571, 572,  
 573, 575, 576, 577, 578, 579, 581, 582,  
 584  
 Roe TM 136, 137, 144, 146, 147  
 Roebuck JD 183  
 Rondeau JA 250  
 Ronningen LD 377, 388  
 Rooney RC 6, 312, 313  
 Roth BJ 3, 4, 105, 202, 205, 206, 207, 208, 226  
 Rovira MJ 8, 208, 327  
 Ruegemer JL 6, 9, 363  
 Ruiz HE 7, 10, 311, 368, 369, 377, 378, 379,  
 384, 388  
 Rumm PD 6, 275  
 Russell CS 4  
 Salerno SM 199  
 Sample SA 137  
 Schachter DT 138, 139, 140, 141  
 Schaefer LA 359  
 Schalhorn SC 8  
 Schall DG 359, 361  
 Schallenberg G 156  
 Scheffler B 2, 3  
 Schempp CM 5, 235  
 Schroeder DW 113  
 Schulte SJ 156  
 Schwartz BF 7, 375, 376, 379, 527, 557  
 Schwartz GH 10  
 Schwartz S 274  
 Schwartz SM 6  
 Scott PT 2  
 Searle CP 121  
 Sekijima J 154  
 Selke S 3  
 Setz S 301  
 Seymour SD 4  
 Shah RB 5  
 Shannon S 267  
 Shaves ME 165, 290, 565  
 Sheffler RL 161, 162, 163, 164, 165, 168, 170,  
 171, 175, 176, 177, 523, 526, 529, 530,

531, 532, 533, 535, 536, 537, 539, 540,  
 541, 543, 545, 546, 547, 549, 552, 554,  
 558, 559, 562, 563, 565, 566, 583, 588,  
 595, 596, 597, 598, 599, 600, 601, 602,  
 603, 604, 605, 606, 607, 608, 609  
 Sheliga V 397  
 Sherman RA 1, 4, 2, 5, 6, 89, 90, 91, 92, 93, 94,  
 95, 96, 97, 98, 99, 124, 210, 240, 241, 243,  
 244, 269, 348, 354  
 Shook ME 2, 76  
 Shrout AB 251  
 Shuhart M 154  
 Sie KC 6  
 Siegel DA 111  
 Sierra RD 517, 518, 522  
 Simmang CL 282, 307, 308  
 Siscovick DS 6  
 Siscovik DS 274  
 Sitler D 313  
 Sluis D 358  
 Smith DV 2, 3, 294, 344, 501  
 Smith PN 249, 270  
 Sneiden S 3  
 Snyder L 145  
 Soderdahl DW 7, 10, 375, 376, 378, 379, 384,  
 388  
 Soma DJ 6  
 Song AU 9  
 Song KM 342  
 Southwell GD 397, 398  
 Sowray PC 516, 522, 523, 526, 529, 530, 531,  
 532, 533, 535, 536, 537, 539, 540, 541,  
 543, 545, 547, 549, 552, 558, 559, 562,  
 563  
 Spence LL 236  
 Sprauge JL 92  
 Staggers M 3  
 Staggers N 217, 221  
 Stajduhar KC 136, 137, 139, 140, 142, 143,  
 144, 146, 147  
 Stankus SJ 8  
 Stapleton LM 160, 161, 166, 167, 168, 169, 171,  
 460, 489, 490, 527, 531, 532, 539, 540,  
 541, 544, 545, 546, 547, 548, 549, 550,  
 551, 553, 555, 557, 558, 559, 560, 561,  
 562, 563, 564, 566, 567, 568, 570, 571,  
 572, 573, 574, 575, 576, 577, 578, 579,  
 580, 581, 582, 584, 585, 586, 587, 588,  
 589, 590, 591, 592, 593, 594, 598  
 Steedman JT 390  
 Steigerwald L 195  
 Stephan MJ 8, 329  
 Stephenson SR 466, 470, 471  
 Stone MD 511, 512, 514, 515, 516, 520, 521  
 StPierre P 338, 352, 353, 355  
 Stracener JC 107, 289, 302, 501  
 Strand JA 521  
 Stredney D 358  
 Strong JS 3, 182, 183, 184, 190, 191  
 Stuart EB 191  
 Stulting RD 324  
 Stutz FH 503, 504, 505, 506, 507, 508, 509,  
 511, 513, 514, 515, 520, 521  
 Styner MJ 1, 2, 76, 82  
 Sudduth RH 10, 157, 158, 183, 190  
 Sweeney JK 263  
 Sweet NL 4, 211, 229  
 Sy FS 2  
 Taillon D 5  
 Tamayo F 397  
 Taquino LT 224  
 Taylor C 66, 67  
 Taylor TO 527, 557  
 Tencer A 7, 121, 342  
 Tenglin RC 160, 166, 174, 460, 532, 539, 544,  
 545, 546, 548, 549, 550, 553, 555, 558,  
 559, 560, 561, 562, 563, 564, 566, 567,  
 568, 571, 572, 573, 575, 576, 577, 578,  
 579, 581, 582, 584  
 Terrio HP 132  
 Thegerge MM 301, 302  
 Thomas KA 224, 232, 233  
 Thomas RW 6, 9, 364, 365  
 Thompson JW 3, 4, 105  
 Thompson S 2  
 Thorndyke Am 280  
 Thrasher JB 6, 7, 10, 169, 174, 370, 371, 372,  
 373, 374, 375, 376, 377, 378, 379, 380,  
 381, 382, 383, 384, 385, 386, 387, 388,  
 389, 390, 391, 527, 542, 557, 569  
 Timmons JH 2, 5, 169, 177, 283, 289, 291  
 Toft CK 2, 3  
 Tollefson DFJ 393, 394  
 Torres MF 8, 9, 330, 331, 332  
 Trementozi DP 264  
 Tries JM 96  
 Tripp GC 247  
 Truxal AR 6, 319, 320  
 Tsuchida AM 5, 155, 156, 157, 158, 183, 190,  
 284, 301  
 Turner BS 222  
 Turner CE 97, 350  
 Twomey PA 389  
 Ulnick KM 10, 366  
 Vaccaro JA 523, 543  
 Vallion RD 160, 161, 166, 167, 168, 169, 171,  
 460, 489, 490, 544, 548, 551, 553, 555,  
 560, 561, 564, 566, 567, 568, 570, 571,  
 572, 573, 574, 575, 576, 577, 578, 579,  
 580, 581, 582, 583, 584, 585, 586, 587,  
 588, 589, 590, 591, 592, 593, 594, 597,  
 598, 599, 602, 604, 605, 608  
 Vandenberg JT 118, 349  
 Vanderlinde TM 270  
 Varma MK 7, 286, 292  
 Vinson DR 1, 108  
 Vonasek LM 98  
 Vorono AA 1, 102  
 Waddell DJ 190  
 Wagner RK 245, 246, 248, 252, 253  
 Waldner DL 360  
 Waldner DT 9  
 Walker WO 277  
 Walsh DW 5, 7, 293  
 Warne WJ 5, 121  
 Watanabe FU 226

Watts DM 308, 314, 315, 316  
 Watts H 3  
 Weaver WD 142  
 Webb CR 4  
 Weber CR 102  
 Wedmore IS 119  
 Weghorst S 358  
 Welch R 342  
 Westphal KA 270  
 Westphal KW 298, 299, 370  
 Wettlaufer JN 5, 7, 384, 391, 527, 557  
 Whitaker MA 7, 294  
 Whitcup SM 6  
 White LJ 6, 8, 321, 326  
 Whitney JD 214, 215, 216  
 Whittemore JB 90  
 Wicks AB 138, 139, 140, 141, 148  
 Wiet GJ 358  
 Wilkerson S 354  
 Willadsen DS 160, 166, 167, 460, 544, 548, 551,  
     553, 555, 560, 561, 564, 566, 567, 568,  
     570, 571, 572, 573, 574, 575, 576, 577,  
     578, 579, 580, 581, 582, 584, 587, 589,  
     590, 591, 592, 593  
 Willard K 339, 340, 348, 354  
 Williams EJ 4, 211, 229  
 Williams JB 5  
 Williams MV 4, 6, 269  
 Williams RF 83, 84, 160, 161, 162, 163, 164,  
     165, 166, 167, 168, 170, 171, 172, 173,  
     174, 175, 176, 177, 489, 490, 551, 553,  
     554, 560, 565, 567, 570, 574, 575, 576,  
     577, 578, 579, 580, 581, 582, 583, 584,  
     585, 587, 588, 589, 590, 591, 592, 593,  
     594, 595, 596, 597, 598, 599, 600, 601,  
     602, 603, 604, 605, 606, 607, 608, 609  
 Williams SC 5  
 Williamson RV 355, 338, 341  
 Williard WC 291, 298, 299, 300, 301, 302, 303,  
     305, 308, 310, 314, 315, 316, 317, 501  
 Wilson LA 114, 115  
 Wilson RM 271  
 Wilson SK 4, 5, 220, 223, 237  
 Wilson SS 2, 3, 208, 290, 524, 552, 565, 586,  
     605  
 Winkle RA 8  
 Winn B 358  
 Winter MG 198, 204, 206  
 Woerman AL 1  
 Wolfe C 143  
 Wong M 1, 2, 5, 91, 92, 95, 99, 348, 354  
 Wood DE 2  
 Woods NF 225  
 Woolman BA 3, 133  
 Wright JR 83, 262  
 Wroblewski KJ 8, 9, 329, 331, 333, 334  
 Yagel R 358  
 Yamamoto K 155, 156, 157, 158, 190, 286  
 Yeager CL 75  
 Yetter JF 134  
 Yoder LH 218  
 Youngberg RA 5, 6, 7, 285, 287, 288, 292  
 Yuill SC 2

Zaichkin J 233  
 Zeh J 3  
 Zimba FA 208, 611  
 Zych KA 277, 279

## KEYWORDS

13-cis retinoic acid 571, 598  
 24 vs 96 hr infusion 455  
 3-D digitizer 357  
 5-Fluorouracil 402, 415, 416, 521, 536, 540, 552  
 5-FU 408, 460, 505, 554, 565, 577, 578, 593,  
     596  
 5FU 574  
 6-Mercaptopurine 469, 470, 481, 482, 496  
 9-cis retinoic acid 428  
 A2 Flexor tendon pulley  
     climbing position 121  
 abdominal radiotherapy 290, 446  
 Abuse  
     child 275  
     spousal 398  
     spouse 275  
 access 210  
 access to care 220  
 accelerated radiation therapy 601  
 acetazolamide 320  
 Achilles tendon 341  
 ACML 474  
 acne 332  
 acromioplasty 346  
 actinomycin D 498, 499  
 Activase Alterplase rt-PA 142  
 active duty women 398  
 adenocarcinoma 405, 546  
 adenoidectomy 361  
 ADHD 279  
 Adolescents  
     military 236  
 adrenomedullin 245, 246, 253  
 Adriamycin 405, 470, 473, 490, 511, 512  
 age 86  
 Agrelin 160  
 air flow obstruction 205  
 airway occlusion pressure 203  
 Akathisia 108  
 albumin 199  
 albuterol 198  
 allogeneic blood therapy 314  
 alpha interferon 576  
 alpha-interferon 529  
 altretamine 422  
 amenorrhea 269  
 aminophylline 144  
 ampicillin 376  
 Anal sphincteroplasty 240  
 anesthesia 101, 193, 339  
 anesthesia care provider 229  
 Aneurysm  
     abdominal aortic 394

angina 143  
 angiotension II 245  
 animal model 114  
 Animal Study 64, 66, 67, 71, 77, 81, 85, 114,  
     115, 248, 249, 260, 291, 306, 307, 308,  
     312, 313, 327, 342, 345, 347, 355, 362,  
     363, 364, 365  
 Ankle 339  
 annual 132  
 anorexia 583  
 antarctic residence 152  
 Anterior cruciate ligament  
     reconstruction 352  
 anti-HER2 454  
 antibodies 81  
 Anticoagulation 186  
 antiemetic 108  
 antigen 582  
 antimicrobial prophylaxis 361  
 aortocoronary 148  
 APFT 122  
 apoptosis 84  
 Appendicitis 305  
 ARA-C 470, 473, 474, 482, 485, 522, 560  
 Arthrodesis 313  
 Arthrography  
     saline 288  
 aspiration 292  
 aspirin 140  
 Asthma 200, 257, 259  
     psychologic adjustment 255  
 Asthmadust mite 256  
 AT 173  
 atelectasis 204  
 ATLS 307  
 Atrial fibrillation 136, 137  
 attitudes 184  
 autoimmune 382  
 autologous cartilage grafting 338  
 azimilide dihydrochloride 141  
 Bacteremia  
     gram positive 315  
 barium enema 284  
 BAY 12-8039 112  
 BCG 380, 507, 511, 518  
 BCG immunotherapy 506  
 BCNU 581, 601  
 Behavior 213, 235  
 Behavior Assessment System for Children 255  
 BEP 409  
 bioabsorbable pins 342  
 bioassay 77  
 biofeedback 96  
 biologic parameters 562  
 biological parameters 513  
 biology 466  
 biology study 488  
 birthweight 86  
 bladder 371, 380  
 bladder cell exfoliation 373  
 bleomycin 407, 409, 417, 486, 543  
 Blood flow 306

finger 95  
 bowel 248  
 blunt trauma 321  
 Bone  
     screw systems 337  
     torsional strength 336  
 bone marrow transplantation 555  
 bone screw 336  
 bovine pericardium 322  
 bowel preparation 183  
 bracing 352  
 bradycardia 144, 147  
 brain metastases 175  
 BRCA1 83, 304  
 BRCA2 173, 304  
 breaking elongation 322  
 breaking load 322  
 Breakthrough pain 163, 165  
 Breast  
     cancer 294  
 Brochoesophagology 362  
 Bronchitis 112  
 bronchogenic 208  
 budesonide 200  
 BUdR 587  
 C-reactive protein 305  
 cachexia syndrome 583  
 CAF 530, 597  
 caffeine 211  
 calcification 191  
 calcium carbonate 553  
 Calcium leucovorin 481, 482  
 can dander 256  
 cancellous trough 353  
 cancer 83, 162, 163, 165, 208, 546, 549, 550,  
     558, 559, 562, 563  
     age 285  
     all types 477  
     AML 485  
     astrocytoma 587  
     biliary 301  
     bladder 310, 372, 381, 511, 518, 523  
     bone 476, 478  
     bowel 506  
     brain 464  
     breast 81, 84, 166, 167, 172, 173, 176, 177,  
         225, 227, 230, 231, 299, 304, 310,  
         501, 505, 509, 510, 513, 514, 530,  
         533, 534, 537, 555, 580, 584, 588,  
         590, 592, 597, 604, 608  
     Burkett's lymphoma 473  
     cervical 408  
     cervix 410, 415, 416, 419, 421, 427, 428,  
         429, 430, 438  
     CNS 471  
     colon 158, 310, 521, 538, 574, 577, 593  
     colorectal 298, 541, 553, 595, 596  
     Dukes B colon 300

endometrial 413, 420, 431, 436, 437, 450, 453  
 endometrium 456  
 esophagus 547  
 Ewing's sarcoma 476, 478  
 germ cell 564  
 glioma 601  
 head & neck 535, 540  
 head and neck 360, 554, 598, 605, 607  
 Hodgkin' disease 486  
 Hodgkin's 487, 503, 561, 567, 570  
 kidney 310  
 larynx 565  
 Leukemia 474, 484, 496, 545, 560, 576, 585  
 location 285  
 lung 170, 175, 310, 512, 575, 579, 582  
     non-small cell 525  
 lymphoblastic leukemia 480  
 lymphoma 468, 573  
 lymphomas 472  
 Medulloblastoma 497  
 meduloblastoma 465  
 melanoma 551  
 metastatic 583  
 myeloma 568, 572, 581  
 nasopharyngeal 536  
 neuroblastoma 466  
 neuroectodermal 476, 478  
 non-Hodgkin's 470, 570  
 non-Hodgkin's lymphoma 480, 504, 507, 515, 589  
 non-small cell lung 171, 548, 571, 586, 594, 602, 609  
 oligodendroglioma 591  
 osteosarcoma 489  
 ovarian 404, 405, 407, 411, 412, 418, 423, 424, 425, 426, 439, 441, 442, 443, 444, 445, 447, 451, 454, 455, 457, 458, 517  
 ovary 422, 452  
 pancreatic 301  
 pediatric 463, 475  
 Pediatric Ewing's 490  
 pediatric rhabdomyosarcoma 492  
 pelvic 401, 403  
 prostate 78, 82, 169, 174, 383, 384, 385, 386, 387, 389, 527, 542, 557, 566, 569, 603  
 rectal 578  
 rectum 460, 552  
 rhabdomyosarcoma 498, 499  
 sarcoma 475, 606  
 soft tissue 285, 476  
 soft tissue sarcoma 495  
 solid tumor 491  
 solid tumors 462  
 testicular 370, 543  
 thymoma 599  
 thyroid 302  
 transitional cell 371  
 transitional cell carcinoma 373  
 undifferentiated sarcoma 499  
 urothelium 600  
 uterine 446  
 uterus 433, 434, 435  
 vagina 429  
 vulvar 440  
 Wilms 488  
 capsular contraction syndrome 333  
 carbon dioxide 291  
 carboplatin 418, 451, 452, 457, 526, 600, 602  
 Carcinogenicity 77  
 carcinoma 408  
 cardiopulmonary bypass circuits 296  
 Carotid endarterectomy 393  
 Carpal tunnel syndrome 129  
 Casts 351  
 Cataract 333  
 CBDCA 526  
 CCNU 497, 587, 591  
 CCU 234  
 cefaxolin 102  
 cell culture system 88  
 cell cycle 84  
 cell line 78  
 cephradine 102  
 Cervical Cancer 449  
 Cervical Carcinoma 448  
 chemo 407, 417, 529  
 chemoendocrine therapy 530  
 chemohormonal therapy 533  
 chemoprevention 553  
 chemoradiation 546  
 chemoradiotherapy 611  
 chemotherapy 164, 458, 471, 472, 484, 488, 506, 508, 509, 514, 517, 519, 520, 524, 528, 533, 537, 538, 541, 543, 555, 558, 580, 586, 590, 592  
     perioperative 574  
 chemotheray 547  
 Child Behavior Checklist 255  
 childbirth  
     faticue 233  
     military 233  
 children 258, 259, 277, 342  
 Cholelithiasis 289  
 CHOP 504, 507, 519, 524, 589  
 chromic phosphate 411  
 chronic myelogenous 576  
 CI-958 425, 443  
 ciprofloxacin 106



circadian timed doxorubicin 437  
 circumferential taping 121  
 cirpofloxacin 376  
 cis-platinum 512  
 cisapride 303  
 cisplatin 162, 168, 171, 406, 407, 408, 409, 412,  
     414, 415, 416, 417, 419, 420, 421, 437,  
     438, 446, 450, 452, 455, 456, 465, 475,  
     497, 525, 526, 536, 540, 543, 554, 565,  
     575, 579, 594, 599, 601, 602, 609  
 cisplatin paclitaxel 447  
 cisplatinum 401, 517, 605  
 civilian husbands 398  
 Clarithromycin 107, 112, 113, 157  
 Clavicle fractures 350  
 Clinafloxacin 179  
 Clinical practice 237  
 clonidine 119  
 collaboration 221  
 colon tumor antigen 158  
 colonoscopy 284  
 Combination 319  
 communication 221  
 completers 396  
 complications 204  
 compression 337  
 computed radiography 191  
 computer aided measurement system 243  
 computer assisted measurements 344  
 Congestive Heart Failure 138, 199  
 consolidation regimens 516  
 Contrast agent 144  
 COPD 105, 198, 394  
 Core biopsy 501  
 corneal curvature 331  
 corneal shape 328  
 corneosclera 321  
 coronary artery disease 191  
 Coronary revascularization 147  
 cortical bone 353, 355  
 corticosteroids 264  
 cost effectiveness 287, 346  
 CoTA test strip 158  
 cotyledon 246  
 coumarin 186  
 CT scan 327  
 CT-Enteroclysis 291, 293  
 CVAD 559  
 cyclophosphamide 405, 409, 412, 457, 470, 476,  
     486, 490, 495, 497, 498, 505, 512, 580,  
     581  
 Cyclosporine 485, 560, 581  
 Cyst  
     bone 312  
     cystectomy 523  
     cytogenetic studies 545  
     cytometry 534, 535  
     cytoreduction 447  
     cytosine arabinoside 469, 481, 522, 585  
     cytoxan 473  
     dactinomycin 409, 431  
 Database  
     medical 126  
     Daunomycin 482, 585  
     daunorubicin 522, 560  
     decannulation 364  
     decision making 213  
     decopensated 139  
     delayed versus immediate repair 341  
     dental facility 92  
     depression 143, 236  
     deslorelin 79  
     Dexamethasone 581  
     dexamethasone acetate 259  
     dexrazoxane 486  
     Diabetes 185  
     diagnostic assays 258  
     diastolic function 188  
     diclofenac 330  
     diet 385  
     dietary supplementation 380  
     dl-Sotalol Hydrochloride 137  
     DNA 75, 534, 535  
     DNA flow cytometry 564  
     dolasetron mesylate 290  
     Domestic violence program 396  
     donor cornea 331  
     dopamine 306  
     dorzolamide 320, 323  
     dose-ranging 194  
     dosing 251  
     doxorubicin 420, 437, 450, 456, 475, 476, 486,  
         495, 561, 580, 581, 590, 592, 608  
     drug therapy 136  
     Duroflo II 296  
     dysphagia 155  
     E. coli asparaginase 469, 482  
     E. coli L-asparaginase 481  
     ear plugs 234  
     eating disorder 269  
     ECG  
         12 lead 110  
     education 128  
     Effectiveness 378  
     efficacy 117, 141, 160, 170, 194, 388  
     EHF receptor levels 582  
     EHOB waffle mattress 218  
     ejection fractions 282  
     electrical nerve stimulation 271  
     electrosurgery 391  
     emergency room 514  
     Emergency surgical procedures  
         training 115  
     Emergency treatment 104  
     emesis 290  
     Endocarditis 179  
     endocrine therapy 537  
     endomyometritis 251  
     endoscopy 248, 249  
     endothelin-1 246  
     enemas  
         hypertonic phosphate 190  
         oral magnesium citrate 190  
         tap water 190

energy restriction 152  
 energy utilization 150  
 Epinephrine Injectable Gel 168  
 episiotomy 240  
 epithelial 455  
 ePTFE 214  
 Erectile dysfunction 388  
 erection vacuum device 375  
 Erwinia aspara 469  
 Erwinia asparaginase 482  
 Erwinia L-asparaginase 481  
 Escimer 325  
 esophageal lesion 155  
 estrogen replacement 436  
 etoposide 403, 409, 417, 427, 434, 476, 486,  
     489, 490, 526, 575, 585, 599  
 Eulexin 384  
 excision 343  
 exercise 188, 244  
 exercise induced 241  
 exercise-induced 122  
 experience 229  
 expiration breathing method 202  
 expression 83, 88  
 external fixation 350  
 extubation 364  
 eye mask 234  
 Factor 8 582  
 familial factors 439  
 family practice 131  
 Fascia lata 322  
 Feeding  
     gastric 226  
     jejunal 226  
 feet 91  
 Female athlete triad 269  
 Female soldiers 123, 243, 273  
     birth outcomes 89  
     pregnancy 270  
 fenretinide 604  
 Fentanyl 111  
 fentanyl citrate 161, 165  
 ferret 114  
 fetal death 262  
 fetal development 262  
 fetus 253  
 fibrin glue 309  
 Field Anesthesia 229  
 Finasteride 569  
 Fingernails 349  
 Fleet enema 183  
 flowsheets 127  
 Flutamide 557  
 FNA 302, 501  
 Foreign bodies  
     intraocular 327  
     intraorbital 327  
     plastic 327  
 Fractures 345  
 Ft Lewis 92, 273  
 Fundulus gardneri 77  
 G-CSF 452, 456, 489, 490, 581, 589  
 Gallbladder 156, 282  
 gastric 546  
 gemcitabine 171  
 Gene KAI1 310  
 genes  
     BRCA1 173  
 genetics 304, 464  
 gentamicin 251, 376  
 GERD 286  
 Glaucoma 319, 320  
 Glenohumeral dislocation 111  
 goat 115, 249  
 goat model 67, 312, 355  
 goats 342  
 Graft markers 148  
 Grafts  
     aorto-coronary 145  
 granulation 364  
 grass pollen 256  
 Growth 343, 363  
     delay 80  
 Gynecologic surgery 248  
 H. pylori 157  
 HCT-OCG 289  
 head & neck 520  
 head circumference 86  
 Headache 92, 94  
     postoperative 211  
 health 270  
 health care report card 217  
 Hearing loss  
     newborns 359  
 Heart Failure 139  
 heart rate control 136  
 heart rhythm control 136  
 Helicobacter pylori 157  
 helium 105  
 HEMASHIELD 393  
 Hematuria 122  
 hemi-femoral turndown 313  
 hemiplegia 196  
 Hemoglobin 182  
 Heparin 146, 296  
 heparin locks 182  
 Herpes simplex 73  
 herpes simplex virus 247  
 high altitude 326  
 high frequency vibration 373  
 histologic grading 584  
 HIV 235, 258, 468, 477  
 Hodgkin's disease 528  
     Stages III & IV 508  
 home exercise program 129  
 home flow rates 379  
 home physical therapy 266  
 homologues 88  
 hormonal manipulation 430  
 hormone refractory 603  
 HPV 430  
 HRCT 286  
 human Steroidogenic Factor-1 88

Hydrocortisone 169, 469, 470, 481, 482  
 hydroxyurea 408, 416, 474, 576  
 hydroxyurea 5-FU 419  
 hyperbaric environment 328  
 Hypertension 306  
 Hypertrophy 188  
 hypochlorite 345  
 hypotension 144, 147  
 hypothyroxinemia 150  
 hysterectomy 410, 421, 438  
 identification 184  
 ifosfamide 414, 446, 473, 475, 476, 489, 490,  
     495, 543, 599  
 IGF 78, 389  
 IL-6 260  
 immune response 264  
 immunity 166  
 immunotherapy 518, 551  
 Incontinence 243  
     anal 242  
 Individual Components 319  
 Infantile spasms 194, 195  
 Infection 345  
     skin 316  
 inflammation 97, 364, 365  
 Inflatable 378  
 Influenza 117, 264  
 Inhaler 206  
 injuries 349  
     combat 348  
     training 348  
 inpatient care 131  
 insole 98  
 inspiration 202  
 inteferon 474  
 Interferon 477  
 interferon-A 531  
 Interferon-alpha 2b 581  
 Interleukin 6 252  
 Interleukin-4 570  
 interleukin-6 490  
 interleukin-g 261  
 Intracranial hemorrhage 261  
 Intraocular pressure 323, 328  
 intrauterine growth 86  
 Intubation 118  
     training 114  
 IP 517  
 iratropium 198  
 Irradiation 487, 561, 577  
 irritative bladder symptoms 381  
 isotope technique 69  
 Itasetron 162  
 IV cyclophosphamide 517  
 IV lines  
     out of hospital 109  
 IV narcotic therapy 250  
 juxta-articular masses 288  
 K-ras 582  
 keratectomy  
     phototherapeutic 321  
 Keratoplasty 331  
 Keratotomy  
     radial 321  
 killer cell activation 227  
 Kinair bed 218  
 kinetic measures 152  
 kinetics 151  
 Knee  
     ganglion 292  
 Korea 273  
 laboratory classification 479  
 lamellar cataracts 329  
 laparoscopy 491  
 laparotomy 411  
 Laryngotracheoplasty 364  
 laser 391  
 Latanoprost 319  
 leiomyosarcoma 434, 435  
 length 86  
 lesions 338  
 letroole 176  
 letrozole 177  
 leucovorin 460, 538, 552, 578, 593  
     high dose 402  
 leucovorin calcium 469  
 leukemia 549, 550  
     lymphoblastic 469, 481, 516  
     non-lymphocytic 522  
     pediatric 469, 479, 482  
     peds 481  
 Levamisole 507, 521, 538, 552, 574, 577, 578,  
     593  
 LH 79  
 lidocaine 111  
 ligation 311  
 linezolid 315, 316  
 lipopolysaccharide 252  
 Lithotripsy 368  
 liver 69, 541  
 localization 357  
 long-term 257  
 Loupe Magnification 369  
 Lovenox 140  
 Low back pain 97, 99  
 low dose vs high dose 596  
 lower limb pain 98  
 lower limbs 91  
 LY320052 (rHb1.1) 314  
 lymph nodes 300, 604  
 lymphadenectomy 410, 438  
 lymphoblastic 496  
 lymphoma 529  
     central nervous system 611  
     non-Hodgkin's 519, 524  
     serum repository 539  
     tissue procurement 532  
 lymphotoxin 445  
 M 519  
 m-BACOD 515, 519  
 M-VAC 523  
 Macrophage 260

Macular edema 330  
 Madigan Army Medical Center 220  
 magnesium citrate 183  
 magnesium oxide 133  
 magnesium sulfate 261  
 malformations 262  
 malignancy  
     pelvic 400  
 mammography 501  
 manipulation 129  
 Mastectomy 309  
 mechanical devices 241  
 medical 66  
 medical facility 92  
 medical resources 280  
 melphalan 406, 581  
 membrane receptors 445  
 memory 150, 279  
 menstrual cycle 244  
 Mental Disorders 184  
 mesna 446, 581  
 Mesodermal Tumors of the Uterus 432  
 Metabolism 262  
     thyroid hormone 152  
 metastatic 444  
 metered dose 206  
 methotrexate 469, 470, 473, 475, 481, 482, 496,  
     505, 512, 581, 611  
 methyl-cellulose 291  
 Microbes 223  
 Microsurgery  
     training 347  
 Migraine 93, 94, 99, 108  
 Military 134, 219  
 Military dependents  
     Korean-born 278  
 military personnel 324  
 military population 275, 397  
 military women 228, 269  
 minocycline 332  
 minors 256  
 mitomycin-C 525  
 mitoxantrone 457, 585  
 mixed mesodermal 433  
 MK-383 146  
 MMPI-2 278  
 modality RX 508  
 modality therapy 509, 547  
 modified NICU 232  
 Molecular biology 74  
 mood 150  
 MOPP 503  
 morbidity 273  
 Morphine 116  
     microencapsulated 71  
 morphine sulfate 163  
 mortality 141  
 MOS 89  
 motor recovery 196  
 Mountain sickness 119  
 mouse 260  
 mouse model 71  
 moxonidine 138  
 MRI 208, 327, 346  
 mRNA transcripts 82  
 MTP-PE 475  
 multidrug resistance 485  
 Muscle  
     leg 133  
     nocturnal cramps 133  
     soreness 271  
 muscle efficiency 150  
 Muscle tension  
     paraspinal 99  
     trapezius 99  
 Musculoskeletal injury 244  
 mycosis fungoides 531  
 myelogenous 550  
 myeloid 549, 585  
 myocardial distribution 283  
 Myocardial infarction 142, 146, 274  
 myocardial ischemia 143  
 Myopia 324, 325  
 nasal mask 205  
 NATRECOR-hBNP 139  
 natural history 349, 510  
 Natural Killer Cell Activation 231  
 nausea 162, 164, 290  
 Navelbine 579  
 neonatal 224  
 Neonates 232  
 Neuralgia 193  
 neurocognitive functioning 277  
 neuropathy 185  
 new technique 283  
 NICU 223, 263  
 nipple-arc-technique 294  
 node positive 597  
 non-gonococcal urethritis 73  
 non-Hodgkin's lymphoma 559  
 non-small cell 575, 579  
 norepinephrine 138  
 Nosocomial pneumonia 212  
 nurses 213  
 Nutropin 80  
 Observation alone 609  
 Ocular hypertension 319, 320  
 Omeprazole 154, 157  
 oncogenes 172, 360  
 Ondansetrom 162  
 ondansetron 164  
 OP physical therapy 266  
 open label 194  
 optic neuropathy 334  
 oropharynx 118  
 Osteochondral defects 338  
 osteogenic sarcoma 563  
 osteoporosis 269  
 Osteotomy 342  
 Otitis media 128, 361  
 out-of-hospital documentation 116  
 outcome 104  
 ovarian ablation 588  
 over age 55 585

overuse 280  
 oxygen 105  
 oxygen therapy 216  
 p105 582  
 P32 412  
 p53 173, 582  
 p53 mutations 300  
 paclitaxel 167, 424, 429, 451, 452, 455, 456,  
     457, 600, 602, 608  
 Pain 116, 311, 390  
     cancer 161  
     cesarean 250  
 palliative management 383  
 Palmaz stent 363  
 Pap smear 132  
 patency 145  
 patient not seen by a physician 104  
 Patient relationship 130  
 patient satisfaction 217, 219, 221  
 pediatric 264, 349, 362, 462, 471, 484, 491, 499  
 PEG asparaginase 482  
 pelvic malignancy 402  
 pelvis 342  
 PEMF 93, 94, 97  
 penicillin G 102  
 penicillin VK 102  
 Penile prosthesis 375  
     Ambicor 378  
 pentoxifylline 583  
 Penumococcus 189  
 perfluorophenanthane 260  
 perioperative local anesthetic 250  
 phacoemulsification 333  
 photorefractive keratectomy 324, 325  
 physeal bars 343  
 Physical fitness 228  
 physical inactivity 274  
 Physical therapy 263  
 Physician 130  
 pig 248, 249, 308, 364  
 pigs 365  
 Pilocarpine 323  
 placebo 119, 140, 154, 390, 583  
 Placenta 245  
 placental cotyledon 252  
 planning 357  
 plasma 253  
 plasma levels 317  
 Plasmodium falciparum 75  
 plaster of Paris 351  
 platinium resistnat 423  
 Platinol 405  
 platinum 426, 458  
 platinum resistant 424, 425  
 platinum sensitive 443  
 Platinum-Sensitive 441, 442, 444  
 pleural effusion 199  
 Pneumonia 113, 181, 226  
 Polar T3 Syndrome 150  
 polymerase 73  
 polyps 284  
 porcine 291  
 positive inguinal nodes 440  
 positive nodes 580, 590, 592  
 positive pressure ventilation 205  
 positive receptors 604  
 Post-MI 141  
 postmenopausal 177, 534  
 postoperative 390  
 postpartum 228  
 potassium 182, 380  
 pramedics 116  
 precocious puberty 79  
 predictors 396  
 predisposition testing 304  
 prednisolone 330  
 prednisone 259, 470, 486, 505, 581  
 Pregnancy 156, 239, 242, 247  
     prevention 125  
         unintended 123, 125  
 premature infants 222  
 premenopausal 533, 588  
 preterm infants 263  
 prevention 385  
 Preventive Medicine 127  
 Primary Care Medicine 134  
 probe covers 223  
 Procarbazine 587, 591  
 prochlorperaine 290  
 prochlorperazine 108  
 professional boundaries 130  
 prognostic factors 597  
 ProMACE-CytaBOM 589  
 ProMACE-Mopp 529  
 Pronation 98  
 proparacaine 193  
 proper use 206  
 prostate  
     resection 391  
 prostate disease 374  
 Prostate specific antigen 374  
 prostatectomy 383, 387  
     perineal 386  
     retropubic 386  
 Prostatitis 376, 382  
 protogen sling 377  
 protein regulation 78  
 Proteins 76  
 Protropin 80  
 Pseudotumor Cerebri 332  
 Pulfrich's phenomenon 334  
 pull-out strength 337  
 pulmonary 286  
 Pulmonary percussive ventilation 204  
 Pulsed Electromagnetic Field Therapy 90  
 Pulsed electromagnetic fields 124, 354  
 Pulsing electromagnetic fields 91, 348  
 purified water 345  
 Purpura  
     thrombocytopenic 277  
 pyelonephritis 106  
 pyrazoloacridine 423, 442  
 QOL 491  
 Quality indicators 217

quality of life 388, 567  
 questionnaire 387  
 questionnaire. body measurements 207  
 quinine 559, 568  
 Radial Keratotomy 325, 328  
     refractive changes 326  
 radiation 172, 450, 465, 565, 594  
 radiation therapy 419, 421, 488, 499, 512, 542  
 Radiculopathy  
     cervical 267  
     lumbar 267  
 radiography 340  
 Radiotherapy 408  
 radiotherapy 410, 413, 415, 420, 460, 471, 497,  
     504, 520, 524, 527, 536, 540, 554, 578,  
     586, 587, 591, 605  
 ras 173  
 rat model 347  
 RB 173  
 recombinant activated protein C 201  
 recurrent 428, 433, 435, 443, 444, 454  
 refraction 328  
 refractory 423, 424, 425, 426, 454  
 reminder 127  
 renal calculi 368  
 reproductive factors 439  
 research 237  
 resection 538, 541, 574  
 Residency training 131  
 rest 188  
 retinoic acid 531  
 Rhabdomyosarcoma 467, 493, 494  
 Rheumatology 187  
 risk factors 212  
 RNA 373  
 Robinow syndrome 329  
 Rotator cuff 353  
 Running  
     deep water 268  
 safety 117, 160, 170, 194, 378, 388  
 saline 345  
 salvage therapy 457  
 scintigraphy 287  
 scoliosis 344  
 Scotchcast Plus 351  
 SDZ PSC 833 424  
 SEBG 82  
 secretions 204  
 sedation 101  
 self-report 279  
 Semmes-Weinstein monofilament 185  
 Sepsis 201  
 seroma 309  
 serum repository 566  
 SHBG 81, 84, 374  
 shin splints 124  
 Sigmoidoscopy 183, 190  
 Simulator  
     ENT 358  
     surgical 358  
 single women 225  
 Sinus rhythm 137  
 Sinusitis 107, 357  
 skill level 229  
 Skin  
     infection 317  
 Skin temperature 224  
 Sleep 234  
 Sleep apnea 207, 366  
 sludge 156  
 small bowel  
     obstruction 293  
 small cell 175, 512  
 SNX-111 390  
 social support 230  
 Society of Thoracic Surgeons 148  
 sodium citrate 380  
 soft tissue 316  
 soft tissue sarcoma 558  
 soft tissue sarcomas 562  
 sparfloxacin 113  
 special clinic 239  
 special operations 66  
 Special Operations Training 67  
 Spouse abuse 397  
 sputum 181  
 squamous cell 427, 428  
 Srugery  
     maxillofacial 101  
 ST segment 143  
 standard chest physiotherapy 204  
 standard radiation 601  
 Stent thrombosis 140  
 stents 364, 365  
 steroid dependent 200  
 Stiff shoulder 266  
 stress 214, 340  
 stress fractures 124  
 stress testing 339  
 stroke 196  
 Subtalar joint 340  
 Suction systems 118  
 sulfamethoxazole 376  
 Suramin 169  
 surfactant 222  
 Surgery 357, 462, 513, 520, 542, 547, 605  
     colorectal 303  
     orthognathic 102  
 Surgical management  
     gynecology 249  
 surgical resection 586  
 surgical staging 404  
 suture ahcnors 355  
 suture retention 322  
 swine 306  
 swine model 362  
 symptoms 187  
 Synercids 317  
 T-cell 480  
 T3(non-radioactive) 151  
 tamoxifen 84, 172, 176, 177, 430, 530, 588, 597,  
     604  
 targretin 170  
 Taxol 590, 592

Teachers 134  
 teen 239  
 Telomerase 75, 76, 301, 302, 370, 371  
 telomerase activity 299  
 telomerase activity 298  
 telomere 372  
 telomere length 299  
 temomerase 372  
 temomere length 298  
 Tendon healing 355  
 tension 94  
 teratoma 407  
 thallium 283  
 thermocouple sensor placement 224  
 Thioplex 175  
 thiotepa 174  
 thrombocytopenia 160  
 thrombosis 186  
 thrombospondin 87  
 thymidylate synthase 595  
 thyroxine 150  
 tibial replacement 313  
 ticlopidine 140  
 tidal volume breathing method 202  
 Timolol 319  
 Timolol Maleate 323  
 tissue procurement 573  
 tissue response 345  
 TNK-tPA 142  
 tolerability 117, 170  
 tomudex 607  
 topotecan 426, 441, 444, 490, 492, 498, 603, 606  
 Toxicology 77  
 Trachea 363  
 Tracheobronchial distention 365  
 tracking 127  
 Training 66, 130  
     endoscopic 308  
     food inspection 64  
     vet techs 85  
 training course 74  
 Training protocol  
     goat 307  
 trans-retinoic acid 576  
 Transbronchial biopsy 202  
 transcripts 88  
 transferrin 214  
 Transfusion therapy 314  
 transient evoked otoacoustic emissions 359  
 transmucosal fentanyl citrate 163  
 treatment program 280  
 triamcinolone acetonide 257  
 TRICARE 219, 220  
 Triiodothyronine 151  
 trimethoprim 376  
 trimetrexate 433, 435  
 troop medical clinic 210  
 Trovafloxacin 107  
 tumor  
     germ cell 526  
     ovary 409  
     ovarian 406  
     ovarian stroma 417  
     sinus 407  
     uterus 414  
 tumor necrosis factor 445  
 Tumors 168  
 Tumour Markers 609  
 tympanostomy tube 361  
 U46619 246  
 Ulcer  
     sclerotherapy 154  
 Ulcer prevention 218  
 ulcers 91  
     feet 354  
     lower limbs 354  
 ultrasonography 240  
 ultrasound 289  
 ureteral calculi 368  
 Urinary flow rates 379  
 Urinary incontinence 96, 210, 241, 377  
 urinary tract 248  
 urine 371  
 uroflowmetry 379  
 uroprotector mesna 414  
 utilization of resources 366  
 VAC 409  
 vaccination 189  
 vaccine 551  
 VAD-P 568  
 Varicocele 311  
 vascular tone 245, 246  
 Vasovasostomy 369  
 ventilation 203  
 verapamil 559  
 VIAGRA 388  
 Viewpoint 357  
 vigabatrin 194, 195  
 vinblastine 561  
 vincristine 409, 438, 473, 486, 490, 495, 497, 499, 505, 512, 581, 587, 591  
 vincristine 498  
 vinorelbine 602, 609  
 visual acuity 328  
 vitamin A 69  
 vitamin B12 189  
 vomiting 162, 164  
 VP-16 418, 465, 473, 512, 594  
 WA 92  
 Waldenstrom's Macroglobulinemia 544  
 washings 371  
 water soluble contrast 291  
 Wilms' 463  
 women soldiers 132  
 Wound healing 87, 90, 214, 216  
     hydration 215  
     oxygenation 215  
 Wrist 287  
 young women 274  
 zanamivir 117  
 Zinecard 487  
 Zoladex 453, 557

## ANNUAL REPORT DISTRIBUTION LIST

Defense Technical Information Center 8725 John J. Kingman Rd. #944 Fort Belvoir, VA 22060-6217	2 copies
Clinical Investigation Regulatory Office ATTN: MCCC-GCI CDR AMEDDC&S 1608 Stanley Road Ft Sam Houston, TX 78234-6125	2 copies
Chief Human Use Review & Regulatory Affairs Division (ATTN: MCMR-RCQ-HR) Office of the Deputy Chief of Staff for Regulatory Compliance & Quality USAMRMC Ft Detrick, Frederick, MD 21702-5012	1 copy
CDR Brooke Army Medical Center ATTN: MCHE-CI Ft Sam Houston, TX 78234-6200	1 copy
CDR Dwight D. Eisenhower AMC ATTN: MCHF-CI Ft Gordon, GA 30905-5650	1 copy
CDR Madigan Army Medical Center ATTN: MCHJ-CI Tacoma, WA 98431	1 copy
CDR Tripler Army Medical Center ATTN: MCHK-CI Honolulu, HI 96859	1 copy
CDR Womack Army Medical Center ATTN: MCXC-FM Box 63H Ft Bragg, NC 28307-5000	1 copy
CDR William Beaumont AMC ATTN: MCHM-DCI El Paso, TX 79920-5001	1 copy
CDR Walter Reed Army Medical Center ATTN: MCHL-CI Washington, DC 20307-5000	1 copy



